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# ANNUAL REPORTS

OF THE

# CHEMICAL LABORATORY

OF THE

# AMERICAN MEDICAL ASSOCIATION

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# ANNUAL REPORTS
OF THE
# CHEMICAL LABORATORY
OF THE
# AMERICAN MEDICAL ASSOCIATION

VOLUME 17-18

JANUARY, 1924—DECEMBER, 1925

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| PART I. . . . . . . . . . | REPRINT OF CONTRIBUTIONS |
| PART II. . . . | REPORTS EXTRACTED FROM THE JOURNAL AND FROM HYGEIA |
| PART III. . . . . | REPORTS NOT PREVIOUSLY PUBLISHED |

PRESS OF
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FIVE HUNDRED AND THIRTY-FIVE NORTH DEARBORN STREET
CHICAGO

# PREFACE

The Chemical Laboratory of the American Medical Association was established in 1906 under the directorship of Prof. W. A. Puckner, to assist the Council on Pharmacy and Chemistry of the American Medical Association in the investigation of proprietary and unofficial non-proprietary medicinal preparations offered to the medical profession.

In accordance with the object of its foundation, the A. M. A. Chemical Laboratory concerns itself primarily with the examination of those proprietary and unofficial medicinal preparations which the Council has under consideration. The Laboratory determines whether the chemical claims made for the composition of these preparations are correctly stated, and, when a product is admitted to the Council's publication "New and Nonofficial Remedies," it looks after the establishment of standards whereby the identity and purity of such a product may be determined.

In addition to the investigations made for the Council on Pharmacy and Chemistry, the Laboratory aids *The Journal of the American Medical Association* in supplying the medical profession and the public with information about the character and composition of drugs. This includes the analyses of proprietary medicinal preparations which are offered to the medical profession and which are not deemed worthy of investigation by the Council on Pharmacy and Chemistry, and the analyses of nostrums ("patent medicines") exploited to the public. Through the columns of The Journal and through direct correspondence the Laboratory responds to requests of physicians for information regarding proprietary preparations advertised to physicians and quack nostrums sold to the public, which have come to their notice. A knowledge of the composition of nostrums, whether offered to the medical profession or to the lay public, is generally a sufficient demonstration that many of the therapeutic claims made for such preparations are unwarranted. For this reason the Laboratory strives earnestly to answer all such inquiries, either by reference to available information or by actual analysis, when it is believed that the results of such investigation will prove of general interest to the medical profession or to the public.

Original investigations along lines which would be of service to the profession at large are undertaken. These investigations are generally reproduced as original articles in *The Journal of the American Medical Association* or in one of the publications of other scientific societies.

In 1924 the Laboratory moved into new quarters. The transfer took place over a period of more than six months, during which time there was considerable delay due to labor difficulties so that the laboratory work for that year was considerably smaller than usual. In view of this it was deemed best not to publish a separate volume for the year 1924 but to include a report of the work done in 1924 with that done in 1925.

This edition of the Reports of the A. M. A. Chemical Laboratory contains, therefore, those portions of the Laboratory's activities during 1924 and 1925 which were believed to be of interest to workers concerned with the examination and standardization of medicines, and includes: (1) reprints of contributions from the Chemical Laboratory of the American Medical Association, (2) reports abstracted from *The Journal of the American Medical Association* and from *Hygeia* and (3) reports not previously published.

It will be appreciated that only a portion of the Laboratory's work can be published in its Annual Reports; this is particularly true in those instances of elaborating standards for New and Nonofficial Remedies, when suggestions of suitable methods or elimination of impurities are results of cooperation (by correspondence) with the manufacturers. Continuing the practice adopted at the foundation of the Laboratory, most of the reports in this volume contain a detailed statement of the analytical methods employed and the results obtained, whenever it was believed that such statement would prove helpful to others engaged in the examination of medicines.

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# PART I

## REPRINTS OF CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION

### CHEMISTRY IN THE SERVICE OF PHARMACEUTICAL MEDICINE *

*(Reprinted from The Journal A. M. A., July 11, 1925, p. 138)*

**Paul Nicholas Leech, Ph.D.**
Director, American Medical Association Chemical Laboratory
CHICAGO

Twenty years ago, chemistry was a June graduate. Today, chemistry is mature, self-supporting and highly respected. It has reached this position of scientific affluence by its attainments not only in its own province, but also, in its interdependencies, including pharmaceutics and medicine. Two decades ago chemistry, trembling, awed, was confronted with theories too fundamental in character to be ignored and by practical problems of vast importance economically. From Denmark had come the Tablets of Stone of the genius Arrhenius, commanding chemists to follow the laws of electric charges, the theory of ions, in order to blast new trails. This in itself was no easy dictum. Equally insistent were the physicists with their applications of electricity; the remarkable findings of Roentgen and the astonishing facts of atomic disintegration presented by the Curies with their work on radium—all had to be adopted. Nor were the practical problems less difficult. There were urgent orders for new chemicals; the automobile industry was demanding new methods of processing steel; the ceramic industry, the oil, the paint, the rubber industries, and a host of others were finding they could no longer make progress by relying on empiricism alone. Almost every endeavor of human progress was looking toward the science of chemistry for aid.

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* Address before American Pharmaceutical Manufacturers Association, White Sulphur Springs, W. Va., June 23, 1925.

Chemistry—baccalaureate chemistry—faced no easy pioneering. It was thus in both Europe and America. But here there were even other demands: public health was receiving unusual attention. The Food and Drugs Act, which was to call for the services of hundreds of chemists and still more for the devising of accurate analytic methods, was being agitated in Congress. To medicine manufacturers the period may be looked on as a mile-stone marking the beginning of a new era of pharmaceutical progress; one which I am sure has been more than welcomed by the representative manufacturers.

It was at this same period, too, that organized medicine created the Council on Pharmacy and Chemistry, to be followed shortly by the installation of the A. M. A. Chemical Laboratory. The chemistry which was aiding agriculturists, which was recreating industry, which was providing the stimulus for university research, was also being called on to advise in the battle against disease. It was to become the pilot to many of the pharmaceutical manufacturers, the adviser to the medical profession, and the watchman of public health. In that field common to both the pharmaceutical manufacturer and to us, what were the conditions as seen in 1905? The domination of Germany in chemical manufacture was supreme. Synthetics were being popularized, the American physician and the laymen alike revering the new synthetics from abroad. They were being introduced in large numbers. As has been said before, it seemed that if a coal tar derivative could not find a place as a dye per se then it surely must have some inherent quality to justify its use as a drug. Synthetic medicinal chemistry in America was neglected. The average American pharmaceutical house either marketed the German drugs in order to make its catalogue complete, or prepared decoctions and tablets mainly from plant substances. In the case even of the remedies sold to physicians, frauds were not altogether uncommon, deception —unintentional or intentional—was rampant, and medical journal advertising teemed with statements concerning the composition of remedies which any chemist familiar with medicines would know were untrue. Such were the conditions as first surveyed by the A. M. A. Chemical Laboratory.

But it has been the fortunate privilege of the A. M. A. Chemical Laboratory to note the improvement wrought year by year by the earnest men of both the medical profession and the pharmaceutical industry. What were the products about which organized medicine sought chemical information as soon as its laboratory was functioning? A good example is "Atoxyl"—the magic drug of that hour. Its chemical composition was presumably declared, but the claims made for it could not go unchallenged. The composition was shown to be wrong, the product not constant from lot to lot, and the declaration of maximum arsenic administration was found faulty when subjected to chemical scrutiny. Be it said to the credit of the firm, however, that when the evidence was shown, the claims were modified. Looking from our perspective today, the criticism is not that these claims in themselves were made, but that the manufacturer of a *chemical* did not have adequate *chemical* advice. "Atoxyl," I believe, was conscientiously exploited; that is, the claims were made in good faith; but if the same claims were made for a similar product today, we would not be so charitable in the statement, because now there is no excuse whatever for lack of competent scientific advice. A more widespread evil was the ethical proprietary with the "paper chemistry formula," impressive, decorative, reflecting discredit on both the house that promoted it and the physicians who prescribed it. The frauds, too, were present; it is only necessary to recall such chemical jokes as zyme-oid and capudine, and others which found the laboratory third degree quite distasteful, though the therapeutic claims cannot be considered so flippantly.

## THE INTERMEDIATE PERIOD

By 1915, ten years later, the change that had taken place was indeed encouraging. Better preparations had been introduced with due consideration of the chemistry. Frauds were relatively rare: only one real outstanding fraud in drugs sold to physicians (I am not speaking of the "patent medicines") do I remember—Syphilodol, the wonderful French antisyphilitic extensively advertised by appealing to the patriotic sentiment and cordial entente between France and the United States. The ampules, beautifully encased, contained nothing more potent than water.

The false statements concerning the composition of many remedies, particularly when made in ignorance, had been modified. There still were a goodly number of secret remedies—so-called ethical proprietaries—which required the attention of the analytic chemist, although their number was lessening.

But the period of greatest stress was during the war. The shortage of German synthetics had to be met, and met it was, but not without difficulty. With praiseworthy efforts, many firms arose to meet this peculiarly chemical emergency. The troubles that occurred in the plants can be told only by those actually engaged in the work at that time, yet it was more than evident that a struggle was going on—lack of competent help, lack of experience. To illustrate: One firm, particularly well known for its excellent work in drug manufacture today, was so handicapped that the A. M. A. Chemical Laboratory had to show the firm the method of making the correct analysis before it could proceed with a satisfactory synthesis. Notwithstanding the hardships, the creative genius of Americans, irrespective of their calling, was evident; again necessity was the mother of invention. It was the privilege of the A. M. A. Chemical Laboratory at this time to aid the Federal Trade Commission, the National Research Council and the Chemical Foundation by passing on the products to be licensed. The Laboratory's aims were to require that the product should not be so pure as to work undue hardship on the American manufacturer, yet to be sufficiently pure to meet the after-the-war competition of the German synthetics. Improvements were suggested which were gladly accepted. In the case of Cinchophen, I well remember how specimen after specimen came in as the process was being improved, until finally a product of sufficient purity was obtained. It was with satisfaction that one noticed this concern or that obtaining the services of men well grounded in fundamentals of science and with high ideals. And their efforts have been reflected in their products. The German supremacy in drug chemistry is no more. Better yet, the example of the Germans has not been followed. The flood of synthetics seems to be an incident of the past. American pharmaceutical chemists are putting out fewer products, with greater likelihood of permanent merit. The work is more thorough. Today there is no foundation in fact for the claim that American chemists cannot make as good products as those imported from abroad.

During the last ten years—the second decade—the A. M. A. chemists have investigated practically all of the better class of drugs placed on the market. In the large majority of instances the product as submitted was all that could be desired *chemically*; its constitution was well worked out, the purity high and the method of assay satisfactory. In some other instances, suggestions for improvement were made which were put in effect. Of course, there were some products to which the Laboratory's attention was called which were far from being what they were claimed chemically. Fortunately, these were not representative products and generally were promoted as lone specialties of a small concern. The products being offered now show that the "June graduate chemist" of 1905 has not ignored his newer conceptions of chemistry; he has applied them to his task and elaborated noteworthy chemotherapeutic agents. (Incidentally, he has increased the difficulties of the chemists serving organized medicine.) The contributions of anesthetics, antiseptics, arsenicals, medicinal dyes, complex diagnostic agents—all these attest the ingenuity of modern chemistry in the service of medicine.

### OPPORTUNITY FOR FURTHER IMPROVEMENTS

The pharmaceutical purveyors, however, are in position to cause some still needed improvements. It is unfair to the better class of firms that there is a group willing to market products of inferior grade, or, worse still, to dispense tablets or preparations that do not contain the declared amount of ingredients, notwithstanding the Food and Drugs Act of 1906. That this is occurring yearly can easily be pointed out by referring to the successful prosecutions instigated by the Bureau of Chemistry.

There is opportunity for improvement in the methods of introducing a drug; to illustrate, in how much better taste was the careful and mature announcement of the chemical work on tryparsamide and insulin than the premature, press-agented story on intarvin. Yet intarvin is of unusual academic chemical interest.

The advertising departments of the pharmaceutical firms, it seems to me, could well afford to cooperate more closely with the scientific workers before copy is sent broadcast. Many of the difficulties that have been dealt with by the Council on Pharmacy and Chemistry and the Chemical Laboratory can be traced to the copy writer. In a recent case at issue, three letters concerning the composition of a product were answered, and answered misleadingly, by the advertising department without once referring the inquiry to the scientific department. The result was a gross deception innocently perpetrated, yes, but inexcusably perpetrated. It is the duty of the A. M. A. Chemical Laboratory to inform the medical profession concerning the composition of drugs. In line with this, the Laboratory published the findings about the product; the firm, quite chagrined, has seen the error and has ordered that in the future all inquiries and even advertising material of such nature must receive the approval of the scientific department, which should have been done at first.

Then take the proposition of names—trade names, therapeutically suggestive names, chemical names that hide the active ingredient. It has been shown in case of the leading drugs of today that names indicative of composition can be coined and used successfully—mercurochrome, butyn, salvarsan or arsphenamine—and many others, names that are distinctive and with a scientific background; yet there are some firms which jeopardize the introduction of a meritorious substance by endowing it with either a foolish name or a therapeutically suggestive name. Also, one needs but pick up many catalogues and note the therapeutic names for various mixtures, particularly tablets, not at all in keeping with the scientific spirit —Antispasmodic Tablets, Carbuncle Ointment, Sciatica Tablets, Brain Sedative and what not. On the other hand, it is gratifying to note that for many years a few houses have listed their tablet mixtures under the correct scientific name.

A suggestion, which has emanated from the pharmaceutical organizations but which has not been adopted generally, is the simplification of the number of dosage forms. Why should there be from thirteen to fifteen different dosages for tablets of arsenous oxide? Does it reflect credit for a firm to clutter up its catalogues with practically every remedy possible simply to appear complete? And not quite so bad, but which in the end is just as futile, is the useless duplication of drugs, the outstanding example of which today is the host of barbital derivatives. Certainly, it is time for the needless products to be discarded.

In this discussion and particularly the suggestions—suggestions made in the spirit of helpful criticism as seen by the A. M. A. chemists—only chemical questions have been involved. Many believe, I have no doubt, that there is still need of modifying therapeutic claims. This is a matter not within the purview of the Chemical Laboratory, a problem that has been dealt with intelligently by the Council on Pharmacy and Chemistry. It may not be amiss to state, however, that a comparison of present day advertising, particularly in medical journals, with that of two decades ago points out more eloquently than words the cooperation the Council has received from the medical profession and progressive pharmaceutical manufacturers. But even so, the matter of therapeutic claims —claims not properly substantiated—still remains the chief task of the Council and of the pharmaceutical house that desires its propaganda to be looked on with favor.

## FUTURE CHEMICAL WORK

The manufacturer and the pharmaceutical chemist both may inquire in what direction chemotherapeutics is to be furthered.

What should be the future tendency of chemistry when enlisted in the service of pharmaceutical medicine?

The present tendency of modern investigators has been in the main copied from two men—Pasteur and Ehrlich. The wonderful accomplishments of Pasteur published fifty years or so ago have been so far reaching in influence and so highly valuable that his work today stands paramount; it may well be questioned whether any single human life has rendered more beneficent service to mankind. The chemists, however, forsook Pasteur—Pasteur the chemist—and allowed others to form a profession distinct from chemistry, and to carry on the remarkable observations of Pasteur with micro-organisms. The bacteriologists claim credit, justly too, for such monuments to human progress as smallpox virus, diphtheria antitoxin and typhoid vaccine. Considered from the chemist's point of view, however, bacteriology has gone about as far as it can. There has been developed a system of fine technic; the life cycle of the organisms as seen under the microscope has been reported with irreproachable accuracy; methods of distinguishing groups, types, strains, have been accurately elaborated. Chemistry, however, has been so busy with its newer conceptions and vast industrial problems that it has not offered the aid to bacteriology and to medicine that it should. One of the problems—it will be largely a pharmaceutical manufacturer's problem in the end—will be to purify the indefinite vaccine, to eliminate it from the shotgun class and to isolate what in our ambiguity we are pleased to call the active principle. That this is necessary, all forward looking scientists will agree, I believe.

Intimately associated with this is the problem of chemotherapy which has been guided by the brilliant contributions of Paul Ehrlich. His theories of drug actions, his themes on avenues of research, have dominated the mind of the present day chemotherapeutic investigator. The quest, despite failures, goes on to find a remedy that will kill the invading organism without seriously injuring the host. But doesn't it often seem that there is much misdirected effort, due to following just this ideal? In the field of chemotherapy can one point to a single remedy that will effectively kill the invading bacteria without unduly injuring the host? Arsphenamine, quinine and mercury, the outstanding examples of chemotherapeutic agents? But their effectiveness is on organisms of a higher type. Success has not been obtained in bacterial invasion. Yet newspapers feature stories, physicians renew interest, pharmaceutical chemists blindly hope whenever an announcement of a new antiseptic is made, particularly if the phenol coefficient is numerically high. The laws of mass action, the electronic theory of oxidation and reduction are not adequately considered. Now this is no deprecation whatever of the work of Pasteur and Ehrlich; it simply makes their contributions all the more remarkable. But it is time to realize that, after all, their work was not in proper sequence. Before bacteriologic chemistry can progress, before chemotherapy can be put on a logical basis, fundamental work must be done on the unit of life, the cell. This need has been recognized for some time. To start work that should have been done many years ago, to go back even farther than Pasteur, relatively speaking, is a difficult suggestion to researchers; to take up an unfinished problem requiring tedious, hard work with no promise of sensational discoveries is not particularly an inducement in this automotive age. But the task is before us, it simply must be done. In doing it, physics especially, and physiology must be at our command. Physics, not alone physical chemistry, including all it does must be utilized in the next decade by all forward-looking pharmaceutical houses engaged in scientific work. In addition to the fundamental studies that must be done on the cell, physics and chemistry must cooperate still further. Drug therapeutists cannot be unmindful of physiotherapy, nor can those who supply physicians with new remedies. After all, physiotherapy is simply another means of inducing chemical reactions in the body. It makes no difference whether cod liver oil, with its deficiency factor, or ultraviolet rays are administered to a rachitic child; the effect is the same. It is somewhat more startling when a chemical such as cottonseed oil is subjected to ultraviolet rays accomplishing the identical results. Bottled sunshine is no longer a fancy. What will be the results of this dicovery in which the surface barely has been scratched, none can fortell. The matter of ionic medication by means of the electric current has not received careful scientific attention, yet it holds forth promise of many interesting observations.

Of course, this fundamental work cannot be done in the laboratories of pharmaceutical concerns; it must be done where there is cooperation of all the sciences, where research will not be hampered by commercial considerations. There is opportunity, nevertheless, for the pharmaceutical industry to recognize that the proper use of drugs will be enhanced by an appreciation of physics and physiotherapy, just as physiotherapy needs the cooperation of chemistry and chemotherapy.

RESEARCH

This leads me to the consideration of research. Of late there have been reports current of a tendency to curtail expenditures on the scientific departments. To do so will probably not be of immediate effect; the dividends might even be increased somewhat for a period. But the pharmaceutical house with competent scientific staff, the concern that encourages research, is the only hope of satisfactory drugs being produced in America. Otherwise the foreign domination of our therapeutics will again return. May that day never be.

## EXAMINATION OF BRANDS OF CINCHOPHEN

### Report of the A. M. A. Chemical Laboratory

*(Reprinted from The Journal A. M. A., Dec. 5, 1925, p. 1829)*

Cinchophen[1] was first described by Doebner and Gieske in 1887; a number of years later it was introduced as a medicine in the United States under the proprietary name "Atophan"

*Cinchophen Examinations*

| Name of Distributor | Cost per Oz.* | Loss on Drying, per Cent. | Ash, per Cent. | Melting Point (Corrected) | Assay, per Cent. |
|---|---|---|---|---|---|
| Abbott Laboratories (*a*) | $1.00 | 0.24 | 0.1 | 211-213 | 99.67 |
| Abbott Laboratories (*b*) | 1.00 | 0.13 | 0.36 | 210-212 | 99.63 |
| Benzol Products Company (*a*) | .... | 0.18 | U† | 212-213 | 99.52 |
| Benzol Products Company (*b*) | 0.50 | 0.055 | U† | 211-212 | 99.80 |
| Calco Chemical Company (*a*) | 1.00 | 0.16 | 0.06 | 212-213 | 99.55 |
| Calco Chemical Company (*b*) | 1.00 | 0.28 | U† | 211.5-213 | 99.10 |
| Mallinckrodt Chemical Works (*a*) | 0.60 | 0.29 | 0.12 | 211.5-212 | 99.52 |
| Mallinckrodt Chemical Works (*b*) | 0.71 | 0.06 | U† | 212-213 | 99.75 |
| Morgenstern & Company (*a*) | 0.80 | 0.12 | U† | 212-213 | 99.15 |
| Morgenstern & Company (*b*) | 0.60 | 0.28 | 0.12 | 210-211 | 99.47 |
| Atophan—Schering & Glatz (*a*) | 2.50 | 0.23 | 0.05 | 214-215 | 99.70‡ |
| Atophan—Schering & Glatz (*b*) | 2.75 | 0.23 | U† | 214-215 | 99.08‡ |

* The price actually paid (including postage in a few instances) when obtained from wholesale dealers in Chicago and in the East.

† Less than 0.5 per cent.

‡ The yellow color of the atophan solution makes it necessary to exercise care, particularly by practice titrations and use of controls, to avoid overstepping the end-point.

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[1] The U. S. P. IX described the product under the name Acidum phenylcinchoninicum (phenylcinchoninic acid). Later the Chemical Foundation and the Council on Pharmacy and Chemistry adopted the coined nonproprietary name "Cinchophen," under which name it is described in the recently issued edition of the Pharmacopeia (U. S. P. X). The chemical name is 2 phenylquinolin-4-carboxylic acid.

by Schering and Glatz, New York, which at that time was the American agent for the firm "Chemische Fabrik auf Actien vorm. E. Schering, Berlin."[2] During the war the proprietary product became quite scarce, but in due time American chemists were synthesizing the needed "phenylcinchoninic acid." The A. M. A. Chemical Laboratory was called on at that time to test the various products. In its report[3] published in 1919 the Laboratory showed that manufacturers had perfected processes so that the products were all good and sufficiently pure to relieve the war scarcity. The melting point, however, which is one of the chief indexes of purity, was still somewhat low. In view of this the laboratory recently reexamined the market supply.

Twelve specimens of cinchophen representing six brands were subjected to the tests prescribed for the U. S. Pharmacopeia X, which becomes official, Jan. 1, 1926. All were odorless; the color ranged from white to a pronounced orange-yellow. The products all responded to the U. S. P. X qualitative tests. The melting point, moisture content, ash and assay (by titration according to U. S. P. X) are given in the accompanying table. The Pharmacopeia requires that the melting point should be about 210 C. In the assay the product is required to be 99 per cent. pure; all the products were found to be above this amount.

Each of the products conformed to all the requirements of the U. S. Pharmacopeia with the unimportant exceptions of color, in one instance, and of ash[4] in another instance. The findings, particularly the melting point, show that the American cinchophen is still purer than in 1918-1919, though at that time it was sufficiently pure for medical purposes. The examination also points out that all products reported on in this paper are equally good for therapeutic purposes, and one is no better than another.

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[2] For a number of years Atophan was included in New and Nonofficial Remedies, but in 1921 the Council on Pharmacy and Chemistry found the product no longer acceptable because of unwarranted therapeutic claims and for other reasons.

[3] Leech, P. N.; Rabak, William; and Clark, A. H.: American Made Synthetic Drugs, II, Examination of Procain, Barbital, Phenetidyl, Acetphenetidin and Phenylcinchoninic Acid Manufactured Under Federal Trade Commission Licenses, J. A. M. A. **73**: 754 (Sept. 6) 1919; Ann. Rep. A. M. A. Chem. Laboratory **12**: 7, 1919.

[4] The U. S. P. X requires that the ash from 0.2 gm. of cinchophen should be negligible. The term "negligible" is defined as a quantity less than 0.0005 gm.; hence the ash from cinchophen should not exceed 0.25 per cent. One specimen of cinchophen-Abbott yielded 0.36 per cent. ash. The ash appeared to consist of sodium sulphate. The two specimens of atophan were somewhat darker in color than prescribed by the U. S. P. X.

[Editorial Note.—The report of the Chemical Laboratory brings out some facts that are directly of interest to the medical profession, and indirectly of interest to the public. It shows, first, that the six brands of cinchophen examined by the methods of the new pharmacopeia are all of good quality. It shows, also, the exorbitant price that the public and the profession have to pay for proprietorship in medicines. Five of the six brands examined are nonproprietary forms of cinchophen. The sixth brand, Atophan, is a proprietary form of cinchophen, no better and no worse than the other five. The report shows that while cinchophen under its nonproprietary pharmacopeial name can be purchased at prices ranging between fifty cents and one dollar an ounce, Atophan costs from $2.50 to $2.75 for the same amount. Obviously there is no justification for such an exorbitant variation. It has frequently been pointed out that the price paid by the public for a "patent medicine" is, on the admission of the "patent medicine" people themselves, enormously over and beyond the fair trade value of the preparations. "Patent medicine" exploiters have virtually admitted that from fifty to seventy-five cents of every dollar charged for a given medicine is expended in advertising the stuff sold. When the physician needs to prescribe cinchophen, his patient will get just as good therapeutic results from a pure cinchophen costing fifty cents an ounce as he will get from an equally pure cinchophen under a fancy name costing $2.75 an ounce. The difference in these wide variations in prices, however, allows the exploiter who sells cinchophen under a trade-marked name to carry on an extensive advertising campaign and hypnotizes the medical profession into the belief that there is some esoteric value in the Atophan brand of cinchophen that does not reside in the non-trade marked cinchophens sold under the pharmacopeial name. As the Bayer concern has given the public the impression that the only genuine aspirin is that put out by it, so the advertising of Schering & Glatz seems to imply that the only genuine cinchophen is put out by Schering & Glatz; "If it's not S. & G.'s, it's not Atophan." This slogan, while technically true, because Schering & Glatz own the trade mark Atophan, is inferentially misleading in that the medical profession is likely to forget that Atophan is merely cinchophen. The way for physicians to show practical disapproval is simple: Prescribe the pharmacopeial cinchophen rather than the proprietary Atophan.]

## EXAMINATION OF SOME LIQUID PETROLATUM AGAR EMULSIONS

*(Reprinted, with additions, from The Journal A. M. A., May 30, 1925, p. 1682)*

**L. E. Warren, Ph.C., B.S.**

During the last year or two a number of preparations have appeared on the market which are said to be emulsions of liquid petrolatum with agar. In addition to these two constituents the preparations are reported to contain one or more of such substances as acacia, glycerin, phenolphthalein, sucrose, sodium benzoate and soluble saccharin.

Some of these petrolatum agar products were submitted to the Council on Pharmacy and Chemistry of the American Medical Association for inclusion with New and Nonofficial Remedies. As the claims made in regard to the composition of one of these emulsions were questioned, the Council requested the Laboratory to examine the product and to work out, if possible, a method of chemical evaluation of the ingredients. In doing this, the investigation of other market preparations of agar petrolatum emulsions was undertaken. The products analyzed were:

Agarol Compound: William R. Warner & Co., Inc.

Agrilin: The Agrilin Co. (Lehn & Fink, Inc., sole distributors, U. S. A.).

Squibb's Liquid Petrolatum with Agar: E. R. Squibb & Sons.

Petrolagar: Deshell Laboratories, Inc.

Terraline with Agar Agar: The Hillside Chemical Co.

Qualitative tests indicated the presence of agar and liquid petrolatum in each preparation, although the liquid petrolatum obtained from "Terraline with Agar Agar" was highly colored and fluorescent. In addition tests were made for each of the other substances which have been reported as present in the various preparations. No product was found to contain all of them. Substances precipitable by alcohol were present in all. Glycerin and sodium benzoate were found in others. Sucrose was found in one, phenolphthalein in one and saccharin in one. Each of the products was of a white, or pale yellowish-white color, except "Terraline with Agar Agar," which was of a pale lemon-yellow color. Each was acid to moistened litmus paper. Each had a mildly sweet taste, except "Agrilin," which was nearly tasteless, and "Terraline with Agar Agar," the taste of which was intensely sweet. Some of the preparations appeared to be flavored with vanilla. The findings obtained in the analysis of the several products are given in the accompanying table.

The adult dose recommended for most of these petrolatum-agar preparations is one tablespoonful twice a day, or one fluidounce daily. Calculation from the analyses shows the quantity of agar and liquid petrolatum that the patient gets by taking any of the preparations examined in its recommended dose.

### AGAROL COMPOUND

The formula for Agarol Compound is not divulged and no claims for its composition are made except that it contains liquid petrolatum and agar (in unstated amounts) and ¾ grain of phenolphthalein in each teaspoonful. It is claimed to be free from "sugar, saccharine, alkalies, alcohol or hypophosphites." Of the several preparations examined, Agarol Compound is the lowest in content of liquid petrolatum. Possibly its low value in this essential may account for its having been reinforced by phenolphthalein. The recommended dose of Agarol Compound of from one-half to one tablespoonful contains from 15 to 30 per cent. of a U. S. P. dose of liquid petrolatum and from 1½ to 3 grains of phenolphthalein. The U. S. P. dose of phenolphthalein is 2½ grains. Based on the analysis, Agarol Compound contains in each tablespoonful about 1 per cent. of a U. S. P. dose of agar.

### AGRILIN

In the report of the Council on Pharmacy and Chemistry refusing Agrilin inclusion with New and Nonofficial Remedies,[1] the composition of the product (in part) as claimed by the manufacturer was given as: liquid petrolatum, 38.6 per cent., and agar, 2.25 per cent. The analysis indicated about 90 per cent. of the claimed amount of liquid petrolatum and about 64 per cent. of the claimed amount of agar. Based on the analysis, each recommended dose of one tablespoonful contains about 37 per cent. of a U. S. P. dose of liquid petrolatum and about 2.5 per cent. of a U. S. P. dose of agar.

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[1] The Journal A. M. A. **84**: 837 (March 14) 1925.

*Analyses of Some Liquid Petrolatum Agar Emulsions*

| | Brand | | | | |
|---|---|---|---|---|---|
| | Agarol Comp. | Agri- lin | Petrol- agar | Squibb | Terraline with Agar Agar |
| Specific gravity, 25/25 C. | 1.001 | 0.984 | 0.916 | 0.991 | 0.933 |
| Loss on drying | 53.7 | 57.6 | 35.2 | 34.3 | 57.1 |
| Liquid petrolatum | 27.0 | 33.2 | 61.0 | 44.7 | 39.8 |
| Specific gravity of liquid petrolatum. | 0.888 | 0.876 | 0.864 | 0.883 | 0.866 |
| Residue not petrolatum | 18.6 | 9.1 | 3.7 | 21.2 | 1.6 |
| Agar (by Squibb method) | 0.6 | 1.4 | 0.3 | 1.3 | 0.3 |
| Substances precipitable by alcohol | 1.3 | 5.2 | 0.6 | 3.7 | 0.4 |
| Sodium benzoate | — | 0.07 | 0.1 | 0.1 | — |
| Phenolphthalein | 1.3 | — | — | — | — |
| Glycerin | 14.9 | 1.9 | — | 14.2 | — |
| Soluble saccharin | — | — | — | — | 0.2 |
| Sucrose | — | — | 2.2 | — | — |

### PETROLAGAR

At the time of its introduction, Petrolagar was claimed to contain "10 per cent. of prepared agar agar" and 65 per cent. of liquid petrolatum. On the request of the Council on Pharmacy and Chemistry that the Deshell Laboratories make a definite, quantitative declaration of the composition of the product, the firm gave the following figures:

| | | |
|---|---|---|
| "Liquid Petrolatum U. S. P. | 65 | c.c. |
| "Agar U. S. P. | 10 | gm. |
| "Sugar and flavoring | 2 | gm. |
| "Sodium Benzoate | 0.1 | gm. |
| "Water to make | 100 | c.c." |

The analysis did not confirm the latter statement.[2] Based on the results of the analysis, each dose of one tablespoonful contains about 65 per cent. of a U. S. P. dose of liquid petrolatum and less than 1 per cent. of a U. S. P. dose of agar. Petrolagar contains the highest proportion of liquid petrolatum of any of the preparations examined, but is relatively low in agar content.

### SQUIBB'S LIQUID PETROLATUM WITH AGAR

Squibb's Liquid Petrolatum with Agar was stated to contain 50 per cent. by volume of liquid petrolatum, 1.5 per cent. of agar, and unstated amounts of acacia and glycerin. These claims were substantially confirmed by the analysis. Each dose of one tablespoonful contains about 50 per cent. of a

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[2] Since the analysis of Petrolagar was made, the firm has informed the Council that the product now being marketed contains 1½ per cent. of agar U. S. P.

U. S. P. dose of liquid petrolatum and about 2.25 per cent. of a U. S. P. dose of agar.

### TERRALINE WITH AGAR-AGAR

No claims are made for the composition of Terraline with Agar Agar except that it is "petroleum purificatum with agar-agar." The petrolatum separated from the preparation in the analysis was not colorless, like the liquid petrolatum from the other preparations examined, but it was colored brownish yellow and possessed a marked fluorescence like lubricating oil. The petrolatum in Terraline with Agar Agar chemically cannot be considered liquid petrolatum of U. S. P. quality. Each recommended dose of the preparation of from one to two teaspoonfuls contains petrolatum equivalent in quantity to from 11 to 22 per cent. of a U. S. P. dose of liquid petrolatum. A dose of the preparation contains from 0.12 to 0.24 per cent. of a U. S. P. dose of agar. The preparation is sweetened with saccharin.

### SUMMARY

The examination reveals that the market preparations of liquid petrolatum with agar vary widely in their content of liquid petrolatum (from 27 to 61 per cent.) and considerably in their agar content. The largest amount of agar in any of the specimens examined was equivalent to about 1.5 per cent. of agar U. S. P.

## Details of Analysis

*Total Solids.*—A weighed quantity of the material was dried on sand on a water bath with occasional stirring with a glass rod. When apparently dry the containers were removed to a vacuum desiccator containing sulphuric acid and allowed to

*Total Solids and Loss on Drying*

| Brand | Weight of Specimen, Gm. | Weight of Residue, Gm. | Percentage of Residue | Average Residue, per Cent | Loss on Drying, per Cent |
|---|---|---|---|---|---|
| Agarol .................. | 1.6930 | 0.7866 | 46.46 | 46.29 | 53.71 |
| | 1.4314 | 0.6601 | 46.12 | ..... | ..... |
| Agrilin .................. | 1.8508 | 0.7939 | 42.35 | 42.32 | 57.68 |
| | 3.8972 | 1.6586 | 42.56 | ..... | ..... |
| | 1.8547 | 0.7803 | 42.06 | ..... | ..... |
| Petrolagar ............ | 2.1448 | 1.3935 | 64.97 | 64.83 | 35.17 |
| | 1.6683 | 1.0825 | 64.88 | ..... | ..... |
| | 1.1591 | 0.7502 | 64.72 | ..... | ..... |
| | 1.5128 | 0.9797 | 64.76 | ..... | ..... |
| Squibb .................. | 1.4657 | 0.9630 | 65.70 | 65.68 | 34.32 |
| | 1.9186 | 1.2599 | 65.66 | ..... | ..... |
| Terraline with Agar.... | 2.3786 | 1.0168 | 42.75 | 42.89 | 57.11 |
| | 2.3060 | 0.9924 | 43.03 | ..... | ..... |

stand over night under reduced pressure. Due to the fact that most of the products contained glycerin constant weight usually could not be attained. The results are, therefore, only approximate. In general, however, the sum of the "petrolatum" and the "total solids not petrolatum" as determined later in the course of the analysis checked fairly well with the "total solids." The "loss on drying" was obtained by subtraction of the "total solids" from 100.

*Liquid Petrolatum.*—About 40 Gm. of the emulsion were weighed in a tared, 100 cc. flask, the flask and contents weighed, the weighed material made up to the mark with water and the flask and contents weighed again. (The specific gravity of the emulsion may be calculated from the values found). The dilution was thoroughly mixed by shaking and 10 cc. transferred to a Röhrer tube by means of a graduate. The volumetric flask was again weighed to determine the weight of the sample taken. The graduate was washed successively with 1 cc. of stronger ammonia water, 10 cc. of alcohol, 25 cc. of water washed ether and 25 cc. of petroleum ether (40 C.—60 C.), the washings being received in the Röhrer tube and the tube shaken thoroughly after each addition. After standing for an hour, the upper layer in the tube was drawn off, the tube being tilted if necessary in order to remove as much as possible of the solvent. The solvent was passed through a 7 cm. filter into a tared Ehrlenmeyer flask of about 100 cc. capacity. To the mixture in the Röhrer tube 15 cc. of ether and 15 cc. of petrolatum benzine * were added and the contents shaken by inverting the tube five times. After standing until clear, the upper layer was drawn off as completely as possible and the solvent, after having been passed through the filter, added to the solvent from the first shake out. A third and a fourth shake out were carried out with 10 cc. each of ether and petroleum benzine,* the filtered solvent being added to the other extracts in the tared flask. Most of the solvent in the combined extracts was recovered by distillation, 1 cc. of alcohol added to the residue, the solvent evaporated by immersion of the flask in a beaker containing boiling water, 1 cc. of anhydrous ether added and the solvent evaporated by immersion of the flask in boiling water for ten minutes. The residue was dried in a partial vaccum over sulphuric acid for 16 hours and weighed. The flask was again placed in the boiling water for 10 minutes, cooled and weighed. If the loss was more than

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* After a quantity of the solvent has been recovered the second and third washing of the aqueous residue in the Röhrer tube may be made with 30 c.c. and 20 c.c., respectively, of the mixed recoveled solvent.

0.01 Gm. from the previous weighing, the treatment with boiling water was repeated.

The presence of phenolphthalein complicates the analysis. The ammonia water does not hold the phenolphthalein entirely in the aqueous-alcoholic solution, so that a portion is dissolved by the ether-petroleum benzine solvent. The difficulty may be overcome by drawing off the solvent containing the liquid petrolatum into a separator and shaking it repeatedly with sodium hydroxide solution until extraction is complete. The solvent hydroxide solution containing the phenolphthalein is then acidified with diluted hydrochloric acid, the mixture shaken repeatedly with small portions of ether, the solvent evaporated and the residue dried at 100 C. and weighed. This weight is to be added to the "total solids not petrolatum" and to the final residues of phenolphthalein obtained later in the analysis.

*Liquid Petrolatum*

| Brand | Weight of Sample, Gm. | Weight of Petrolatum, Gm. | Percentage of Petrolatum | Average Petrolatum |
|---|---|---|---|---|
| Agarol | 4.0543 | 1.0921 | 26.94 | 27.06 |
| | 4.0543 | 1.1038 | 27.18 | ..... |
| Agrilin | 3.7639 | 1.2648 | 33.60 | 33.24 |
| | 3.7639 | 1.2547 | 33.33 | ..... |
| | 7,5278 | 2.4689 | 32.79 | ..... |
| Petrolagar | 4.0332 | 2.4595 | 60.98 | 61.02 |
| | 4.0285 | 2.4515 | 60.85 | ..... |
| | 4.0313 | 2.4925 | 61.82 | ..... |
| Squibb | 4.5594 | 2.0403 | 44.74 | 44.69 |
| | 4.5589 | 2.0353 | 44.64 | ..... |
| Terraline with Agar | 6.7802 | 2.7096 | 39.96 | 39.79 |
| | 6.4442 | 2.5568 | 39.62 | ..... |

*Solids Not Petrolatum.*—The liquid remaining in the Röhrer tube after removal of the liquid petrolatum was transferred to a tared beaker. Particles of jelly-like material adhering to the sides of the tube were removed by washing with water and rubbing with a long, rubber tipped rod slightly bent at the distal end. The aqueous liquid was evaporated nearly to dryness on the water bath, the residue dried over sulphuric acid in a partial vacuum for sixteen hours and weighed. This weight represents "total solids not petrolatum." If phenolphthalein were present in the original material a correction must be added, equivalent to the phenolphthalein dissolved by the liquid petrolatum as noted in the preceding paragraph.

*Solids Not Petrolatum*

| Brand | Weight of Specimen, Gm. | Weight of Residue, Gm. | Percentage of Residue | Average Residue |
|---|---|---|---|---|
| Agarol | 4.0543 | 0.7603 | 18.75 | 18.62 |
| | 4.0607 | 0.7505 | 18.48 | ..... |
| Agrilin | 3.7639 | 0.3435 | 9.12 | 9.09 |
| | 3.7639 | 0.3411 | 9.06 | ..... |
| Petrolagar | 4.0332 | 0.1461 | 3.62 | ..... |
| | 4.0285 | 0.1581 | 3.80 | ..... |
| | 4.0313 | 0.1505 | 3.73 | 3.72 |
| Squibb | 4.5594 | 0.9732 | 21.34 | ..... |
| | 4.5589 | 0.9632 | 21.13 | 21.24 |
| Terraline with Agar | 6.7802 | 0.1088 | 1.65 | ..... |
| | 6.4442 | 0.1016 | 1.58 | 1.61 |

*Agar.*—The residue obtained as described in the preceding paragraph was treated with 20 cc. of water, the mixture stirred occasionally with a glass rod for three hours and allowed to stand over night. The mixture was transferred to a tared Gooch crucible, the insoluble material washed with three portions of 5 cc. each of cold water, the residue dried at 100 C. to constant weight and weighed.

*Agar*

| Brand | Weight of Sample, Gm. | Weight of Agar, Gm. | Percentage of Agar | Average Agar |
|---|---|---|---|---|
| Agarol | 4.0543 | 0.0238 | 0.587 | 0.58 |
| | 4.0607 | 0.0234 | 0.576 | .... |
| Agrilin | 3.7639 | 0.0525 | 1.39 | 1.43 |
| | 3.7639 | 0.0551 | 1.47 | .... |
| Petrolagar | 4.0285 | 0.0140 | 0.37 | .... |
| | 4.01313 | 0.0133 | 0.33 | 0.35 |
| Squibb | 4.5594 | 0.0594 | 1.30 | 1.30 |
| | 4.5589 | 0.0591 | 1.29 | .... |
| Terraline with Agar | 6.7802 | 0.241 | 0.355 | 0.33 |
| | 6.4442 | 0.197 | 0.305 | .... |

*Substances Precipitable by Alcohol.*—The filtrate obtained from the determination of agar was evaporated to about 5 cc., sufficient alcohol added, a few drops at a time with shaking, to render the solution faintly turbid and the mixture poured with stirring into 100 cc. of cold alcohol. The mixture was transferred to the original beaker with stirring, using a few cubic centimeters of alcohol for washing, and the mixture allowed to stand over night. The precipitate was collected in a tared Gooch crucible, washed with cold alcohol, dried at 100 C. to constant weight and weighed.

*Substances Precipitable by Alcohol*

| Brand | Weight of Specimen, Gm. | Weight of Gum, Gm. | Percentage of Gum | Average |
|---|---|---|---|---|
| Agarol | 4.05434 | 0.0505 | 1.24 | 1.33 |
| | 4.06074 | 0.0573 | 1.41 | .... |
| Agrilin | 3.7639 | 0.1925 | 5.12 | .... |
| | 3.7639 | 0.1975 | 5.25 | 5.23 |
| | 7.5278 | 0.4022 | 5.32 | .... |
| Petrolagar | 4.0285 | 0.0263 | 0.65 | .... |
| | 4.0332 | 0.0192 | 0.47 | 0.56 |
| Squibb | 4.5594 | 0.1695 | 3.72 | .... |
| | 4.5589 | 0.1690 | 3.70 | 3.71 |
| Terraline with Agar | 6.7802 | 0.0244 | 0.36 | 0.37 |
| | 6.4442 | 0.0252 | 0.38 | .... |

*Residue Not Petrolatum, Agar or Acacia.*—Most of the alcohol in the filtrate from the acacia determination was recovered by distillation, the remainder evaporated on a water bath and the residue dried in a partial vacuum over sulphuric acid to approximately constant weight. This is considered as "residue not petrolatum agar or acacia."

*Residue Not Petrolatum, Agar or Acacia*

| Brand | Weight of Specimen, Gm. | Weight of Residue, Gm. | Percentage of Residue | Average Residue |
|---|---|---|---|---|
| Agarol | 4.0543 | 0.6728 | 16.59 | 16.27 |
| | 4.0607 | 0.6479 | 15.95 | ..... |
| Agrilin | 3.7639 | 0.0667 | 1.77 | 1.96 |
| | 3.7639 | 0.0763 | 2.03 | ..... |
| | 7.5618 | 0.1571 | 2.08 | ..... |
| Petrolagar | 4.0285 | 0.1156 | 2.87 | 2.88 |
| | 4.0332 | 0.1164 | 2.88 | ..... |
| Squibb | 4.5594 | 0.6495 | 14.22 | 14.32 |
| | 4.5589 | 0.6575 | 14.42 | ..... |
| Terraline with Agar | 6.7802 | 0.0145 | 0.214 | 0.31 |
| | 6.4442 | 0.0261 | 0.405 | ..... |

*Glycerol, Soluble Saccharin, Phenolphthalein, Sodium Benzoate, Sucrose, Etc.*—The residue, "not petrolatum, agar or acacia," was taken up in the water, the solution acidified with hydrochloric acid and the mixture shaken repeatedly with ether until extraction was complete. The bulked ether extractives were washed with water and the solvent evaporated in a tared dish to apparent dryness. The residue was dried over sulphuric acid in a partial vacuum to constant weight. The benzoic acid obtained was calculated to sodium benzoate and the saccharin to sodium saccharin. The weight of the sodium benzoate and soluble saccharin as well as the phenolphthalein was subtracted from the weight of the residues "not petrolatum, agar or acacia" and the remainder considered as glycerin.

*Phenolphthalein, Sodium Benzoate or Saccharin*

| Brand | Weight of Specimen, Gm. | Weight of Ether Extract, Gm. | Percentage of Ether Extract | Average | Sodium Benzoate or Soluble Saccharin |
|---|---|---|---|---|---|
| Agarol ................. | 4.0543 | 0.0575 | 1.41 | 1.33 | ..... |
| | 4.0607 | 0.0501 | 1.24 | ..... | ..... |
| Agrilin ................. | 3.7639 | 0.0030 | 0.08 | 0.06 | 0.07 |
| | 7.5278 | 1.0025 | 0.03 | ..... | ..... |
| Petrolagar ............. | 4.8562 | 0.0047 | 0.097 | 0.097 | 0.114 |
| Squibb ................. | 4.5594 | 0.0039 | 0.085 | ..... | ..... |
| | 4.5589 | 0.0042 | 0.092 | 0.088 | 0.104 |
| Terraline with Agar..... | 6.7802 | 0.0097 | ..... | 4.14 | ..... |
| | 6.4442 | 0.0084 | ..... | 0.13 | 0.18 |

*Glycerin (by Calculation)*

| Brand | Percentage of Residue Not Petrolatum, Acacia or Agar | Percentage of Sodium Benzoate, Soluble Saccharin or Phenolphthalein | Percentage of Glycerin |
|---|---|---|---|
| Agarol ........................ | 16.27 | 1.33 | 14.94 |
| Agrilin ....................... | 1.96 | 0.07 | 1.89 |
| Petrolagar .................. | 2.88 | 0.114 | Absent; contains sucrose |
| Squibb ........................ | 14.32 | 0.104 | 14.22 |
| Terraline with Agar......... | 0.31 | 0.18 | Absent |

*Sucrose.*—The aqueous-acid solution, after removal of the benzoic acid, phenolphthalein or saccharin by ether, was evaporated to about 20 cc. to remove ether and to invert the sucrose, the solution was neutralized with sodium hydroxide solution and the reducing sugars determined by the Munson and Walker method of the A. O. A. C. (Methods of Analysis, pp. 78 and 321, 1919). The results were calculated to sucrose: Petrolagar was the only specimen which contained sucrose.

*Sucrose*

| Brand | Weight of Specimen, Gm. | Weight of $Cu_2O$, Gm. | Equivalent of Sucrose, Gm. | Percentage of Sucrose | Average per Cent of Sucrose |
|---|---|---|---|---|---|
| Petrolagar ... .... | 1.9401 | 0.1002 | 0.04275 | 2.20 | 2.23 |
| | 6.7904 | 0.3385 | 0.15319 | 2.26 | .... |

# THE COMPOSITION OF SOME COMPLEX BISMUTH TARTRATES USED IN THE TREATMENT OF SYPHILIS*

*(Reprinted from the Journal of the American Pharmaceutical Association, Vol. XIV, No. 6, June, 1925, p. 478)*

**By L. E. Warren, Ph.C., S.B.**

During the past several years a number of complex bismuth compounds have come into use in the treatment of syphilis. Their use in this disease originated in France and the majority of the pharmacological and clinical tests with these compounds have been carried out by French investigators. However, several reports have appeared in American journals.

Comprehensive reviews of the literature concerning the use of bismuth compounds in syphilotherapy[1] have appeared from time to time, so that they need not be repeated here and American chemical manufacturers have been producing some of the preparations used. The compounds commonly employed are stated to be potassium sodium bismuth tartrate, potassium bismuth tartrate and to a lesser extent, bismuth oleate, quinine bismuth iodide and finely divided metallic bismuth. Some tests have been carried out with bismuth citrate, bismuth trioxide and a few other bismuth compounds.

There is considerable confusion in the literature concerning the composition of the so-called bismuth tartrates used in the treatment of syphilis. Robert and Sauton,[2] who were the first to experiment with the bismuth tartrates in syphilis of animals, state that they used "sodium bismuth tartrate" which they prepared by the method published by Cowley.[3] The preparation which has been most used in France is claimed by Sazerac and Levaditi[4] to be potassium sodium bismuthotartrate, and to be prepared also by the method given by Cowley.[3] It is sold in an oily suspension under the name of Trepol. An examination of Cowley's paper reveals that the product which might be expected from the reaction which he described probably would not be potassium sodium bismuth tartrate, but previous to solution in sodium hydroxide (which he directs as part of the process) would be more likely to be a basic bismuth tartrate. This will be discussed more fully later. The error of calling this product a "potassium sodium bismuth tartrate" has continued in the literature unchallenged.

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* An abstract of this paper was published in THE JOURNAL A. M. A., April 4, 1925, p. 1067.

[1] J. A. M. A. **82**: 661, 1923; ibid. **83**: 2087, 1924; Am. J. Syph. **7**: 352, 1923.

[2] Robert, A. E., and Sauton, B.: Action du bismuth sur la spirallose des poules, Ann. Inst. Past. **30**: 261, 1916.

Bismuth tartrate compounds appear to have been first described by Schwarzenberg in 1847.[5] Since then a great variety of compounds of bismuth with tartaric acid have been prepared. The composition of the finished products appears to vary with the method of manufacture, slight deviations in procedure apparently being responsible for considerable differences. Some of these compounds are briefly mentioned herewith. Following Schwarzenberg, Schneider[6] in 1853 prepared a variety of bismuth compounds including a basic bismuth tartrate.

In 1866 Frisch[7] described a potassium bismuth tartrate to which he assigned the formula $K\ BiC_8H_2O_{12}$.

In 1894 Fischer and Grützner[8] prepared what they termed a neutral and an acid bismuth tartrate. The formulas ascribed to these compounds were respectively $C_4H_4O_6.2Bi(OH)_2$ and $Bi(OH)_2.C_4H_5O_6$.

Baundran has described a variety of compounds of tartaric acid with bismuth and potassium.[9]

Rosenheim and Vogelsang[10] discuss the constitution of potassium bismuth tartrate. The formula which they assign to the product is

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[3] Cowley, R. C.: Organic Salts of Bismuth with Alkalies, Chem. & Drug **82**: 212, 1913.

[4] Sazerac, R., and Levaditi, C.: Action du bismuth sur la syphilis et sur la trypanosomiase du Nagana, Compt. rend. acad. sci. **172**: 1391, 1920.

[5] Schwarzenberg, A.: Ueber eine Verbindung von Wismuthoxyd, Kali und Weinsteinsäure, Ann. Chem. Pharm. **61**: 244, 1847.

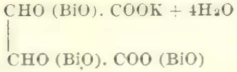
[6] Schneider, R.: Untersuchungen über das Wismuth, Ann. Phys. Chem. **88**: 45, 1853.

[7] Frisch, K.: Ueber die Basicitat der Weinsaure, Jour. prakt. Chem. **97**: 278, 1866.

[8] Fischer, B., and Grützner, B.: Ueber die Basicitat der Weinsäure, Arch. Pharm. **232**: 462, 1894.

[9] Baundran, P.: Étude sur les émétiques, Ann. chem. phys. [7] **19**: 536, 1900.

[10] Rosenheim, A., and Vogelsang, W.: Ueber einige Salze und Komplexsalze des Wismuts, Ztschr. f. anorg. Chem. **48**: 205, 1906.



$$\begin{array}{l}\text{CHO (BiO). COOK} + 4H_2O\\ |\\ \text{CHO (BiO). COO (BiO)}\end{array}$$

This compound should theoretically contain 67.15 per cent of bismuth and 4.21 per cent of potassium.

Greco and Muschietti[11] prepared potassium sodium bismuth tartrate for their use by treating bismuth oxide with a warm solution of tartaric acid adding an aqueous solution of potassium tartrate, after warming on the water bath for an hour, and finally neutralizing with an aqueous solution of sodium hydroxide, using phenolphthalein as indicator. The product was dried on porcelain plates and preserved in bottles out of the light. It was a white powder which contained 48 per cent of bismuth. These authors assign the formula KCOO.CHOH : CHOBiO.COONa to the compound.

Calcagno[12] disagrees with Greco and Muschietti and believes that the formula of the product should be $KCOO\ (CHOH)_2\ (COO)_2\ (BiO)_2\ (CHOH)_2\ COONa + H_2O$. The formula maintained by Calcagno theoretically should contain about 33.8 per cent of bismuth.

Greco[13] replied to Calcagno at some length and Calcagno[14] replied to Greco, each maintaining the correctness of his first contentions but without adding anything of consequence to the discussion.

Fabregue[15] prepared a bismuth tartrate by dissolving bismuth nitrate in acetic acid, adding an aqueous solution of sodium tartrate, washing the resultant, white precipitate with alcohol and drying it at 60°. The product was a white, microcrystalline powder; insoluble in water but soluble in ammonia water.

Only very few analyses of potassium sodium bismuth tartrate or similar compounds have been reported. In 1922 Barthe[16] analyzed two commercial specimens of potassium, sodium bismuth tartrate. They were claimed to have the formula KOOC.CHO (BiO) CHOH.COONa. A compound having this formula theoretically contains 48.02 per cent of bismuth. Barthe found 48.04 and 63.41 per cent of bismuth respectively.

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[11] Greco, N. V., and Muschietti, A. H.: El Bismuto en el tratamiento de la sifilis, Sem. med. **28**: 849, 1921.

[12] Calcagno, O.: A propósito del Tartrobismutato Sodicopotásico, Sem. med. **29**: 5, 1922.

[13] Tartrobismutato Sodicopotásico, ibid. 64.

[14] Tartrobismutato Sodicopotásico, ibid. 95.

[15] Fabreugue, M.: Sur une mode de préparation du citrate et du tartrate de bismuth, J. pharm. chim. [7] **25**: 341, 1922.

[16] Barthe, L.: Le tartrobismuthate de potassium et de sodium, Bull. Soc. pharm. Bord. **60**: 20, 1922.

Klauder and Raiziss[17] state that they have examined several commerical samples of potassium sodium bismuth tartrate (brand names not given) and have found less than 52 per cent of bismuth. The potassium salt which Klauder employed clinically was found by Raiziss to contain about 62 per cent of bismuth. The potassium content was not determined.

Hopkins[18] prepared by the Cowley[3] method what he calls the "quadruple salt" *i.e.*, potassium sodium bismuth tartrate. His analyses (made by Dr. J. H. Mueller) showed 54.2 per cent of bismuth but neither sodium nor potassium were determined. This compound will be referred to again.

In making a study of some of the commercial bismuth salts used in the treatment of syphilis, the first experiments made in the Chemical Laboratory A. M. A. were undertaken with the view of gaining some information concerning the composition of the compound made by the Cowley process.[3] Accordingly a quantity of the salt was prepared by his method with the modification that the precipitate was dried at 100° instead of being dissolved in sodium hydroxide solution as Cowley directs. The yield from 70 Gm. of bismuth subnitrate was 81 Gm. of the dried product.

Cowley[3] prepared his complex bismuth salt as follows:

| | |
|---|---|
| Bismuth subnitrate | 70 Gm. |
| Potassium sodium tartrate | 64.5 Gm. |
| Nitric acid (specific gravity, 1.430) | 57 cc. |
| Sodium bicarbonate | 57 Gm. |

> Mix the nitric acid with an equal volume of water and dissolve the bismuth subnitrate in the mixture. Add the Rochelle salt dissolved in a little water and then the sodium bicarbonate also dissolved in water. Heat to expel carbon dioxide, filter and wash the precipitate until the filtrate no longer gives a test for nitrates. Lastly dissolve the precipitate in normal sodium hydroxide solution.

It appears probable that the precipitate produced by this reaction is a basic bismuth tartrate insoluble in water but soluble in sodium hydroxide solution. Cowley called his finished product "a solution of sodium bismuth-tartrate" and never at any time claimed it to be a potassium sodium bismuth tartrate. From the rather indefinite statements in the literature, it would seem probable that the active substance in Trepol is the basic bismuth tartrate as prepared by Cowley (before solution in sodium hydroxide) and that it is not a

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17. Klauder, J. V., and Raiziss, G. W.: Bismuth in the Treatment of Syphilis, Arch. Derm. & Syph. **7**: 721, 1923.

18. Hopkins, J. V.: Bismuth in the Treatment of Syphilis, Arch. Derm. & Syph. **7**: 745, 1923.

potassium sodium bismuth-tartrate as is claimed by the French manufacturers and clinicians. This (the insoluble salt) is the preparation used by Hopkins in this country[18] (mentioned earlier in this paper) but Hopkins calls his preparation the "quadruple salt," evidently believing that it contains both potassium and sodium. In a later paper Hopkins[19] refers to this compound as the "potassium sodium bismuth tartrate (soluble)" but gives no clew to his method of rendering the substance soluble.

Klauder[2] employed "the potassium salt because" he states "its chemical constitution is probably more definite, its preparation easier, and because its spirocheticidal action was regarded as efficient as the 'sodium potassium tartrobismuthate' which is probably a mixture of the potassium and sodium salts." This salt contained 62 per cent of bismuth.

### LABORATORY SPECIMEN

After being passed through a No. 30 sieve, the compound prepared in the laboratory by the Cowley[3] method was a white, finely granular, odorless powder. It was insoluble in water but soluble in dilute alkalies; soluble in acids without effervescence. On exposure to air for several days, a weighed sample of the salt gained about 2.3 per cent of its weight. The compound was submitted to analysis by the following method:

> *Bismuth.*—A weighed quantity of the bismuth salt was dissolved by agitation in weak ammonia water, the bismuth precipitated as bismuth sulphide from the warmed solution by hydrogen sulphide, the precipitate collected in a weighed Gooch crucible, washed successively with water, alcohol, ether, carbon disulphide, alcohol and ether in the order named, dried at 100° and weighed.

In three determinations the weight of the bismuth sulphide obtained corresponded to 60.64, 60.97 and 61.83 per cent of bismuth, respectively.

> *Tartaric Acid.*—The filtrate from which the bismuth sulphide had been removed was slightly acidulated with hydrochloric acid, the solution evaporated to half its volume, the residue placed in a graduated flask and made up to volume. An aliquot portion of the solution was evaporated to about 25 cc., an excess of potassium chloride added, followed by 2 cc. of glacial acetic acid and, after stirring, two volumes of alcohol. After standing over night the precipitate (potassium bitartrate) was collected in a Gooch crucible and washed with 50 per cent alcohol until free from acetic acid. The crucible was then placed in

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[19] Hopkins, J. V.: Antisyphilitic Action of Bismuth, J. A. M. A. **83**: 2087, 1924.

> a beaker containing hot water and the acidity titrated with normal sodium hydroxide, using phenolphthalein as indicator. The results were calculated to tartaric acid, $H_2C_4H_4O_6$.

The results of two determinations were, respectively, 32.0 per cent and 31.9 per cent of tartaric acid.

> *Potassium and Sodium.*—An aliquot portion of the diluted filtrate from the bismuth determination was evaporated to dryness in the presence of an excess of sulphuric acid, the residue heated to low redness, cooled, a fragment of ammonium carbonate added and the residue again heated. The mixture of potassium sulphate and sodium sulphate was weighed, its sulphate content determined as barium sulphate in the usual way and the relative proportions of potassium and sodium calculated by the method described in the reports of the Chemical Laboratory A. M. A. vol. 6, p. 44, 1913.

The results from two determinations were 0.34 per cent and 0.22 per cent for potassium and 0.34 per cent and 0.30 per cent for sodium.

A salt having the composition $K_3Na_3Bi_2O_{16}H_{12}O_{24}$[20] when dried should contain 34.95 per cent of bismuth, 9.85 per cent of potassium and 5.80 per cent of sodium. According to the Powers, Weightman, Rosengarten Co., this compound should be soluble in water. It is very evident that a salt insoluble in water and containing 61 per cent of bismuth and considerably less than 1 per cent of total potassium and sodium, cannot be correctly called a "potassium sodium bismuth tartrate." Therefore, it is concluded that the salt prepared by Cowley's method as modified in the A. M.A. Laboratory is not a potassium sodium bismuth tartrate, but is, essentially, a bismuth tartrate containing small amounts of potassium and sodium compounds as impurities. A comparison between the formula suggested by the Powers, Weightman, Rosengarten Co., as well as the formulas for some other theoretical compounds, and the findings for the laboratory specimen are given in the following table:

TABLE 1.—*Comparison of a Laboratory Specimen of Bismuth Tartrate with Theoretical Formula*

| Theory | Potassium | Sodium | Bismuth | Yield of Tartaric Acid | Water of Hydration |
|---|---|---|---|---|---|
| $KNaBiC_4H_3O_7$ | 9.02 | 5.31 | 48.02 | 34.6 | .... |
| $KNaBiC_8H_8O_{14}\cdot H_2O$ | 6.34 | 3.73 | 33.75 | 48.7 | 2.92 |
| $K_3Na_3Bi_2C_{16}H_{12}O_{24}$ | 9.85 | 5.80 | 34.95 | 50.4 | .... |
| Laboratory Specimen | 0.28 | 0.32 | 61.1 | 32.0 | 0 |

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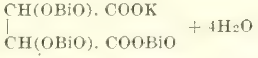
[20] This formula was suggested by the Powers, Weightman, Rosengarten Co. It is again referred to in this paper.

### SPECIMEN FROM DERMATOLOGICAL RESEARCH LABORATORIES

A specimen of potassium bismuth tartrate was received from the Dermatological Research Laboratories. It was a white, odorless powder, easily soluble in water. The aqueous solution had a very faintly alkaline reaction to litmus and gave precipitates with solutions of a number of alkaloidal salts and local anesthetics. The manufacturer stated that the compound was believed to have the composition approximately represented by the formula:



$$\begin{array}{l}\mathrm{CH(OBiO).COOK} \\ | \\ \mathrm{CH(OBiO).COOBiO}\end{array} + 4H_2O$$

A compound having the formula indicated theoretically should contain 67.15 per cent of bismuth, 4.21 per cent of potassium and 7.75 per cent of water of hydration. Evidently this preparation is intended to correspond to that described by Rosenheim and Vogelsang.[10] Analysis by the method used in the examination of the specimen prepared in the laboratory, omitting the treatment with ammonia water to produce a solution, gave 65.73 per cent of bismuth, 5.26 per cent of potassium, 20.5 per cent of tartaric acid liberated and 4.53 per cent of water of hydration. The examination indicates that the composition of the product is essentially as claimed by the manufacturer. A comparison of the theoretical composition with the findings is shown in Table 2.

Table 2.—*Analysis of a Specimen of Potassium Bismuth Tartrate Compared with the Theoretical Formula*

| Theory for | Potassium | Bismuth | Tartaric Acid Liberated | Water of Hydration |
|---|---|---|---|---|
| $KBi_3C_4H_2O_9 + 4H_2O$ ......... | 4.21 | 67.15 | 16.15 | 7.75 |
| D. R. L. Specimen............. | 5.26 | 65.73 | 20.50 | 4.53 |

Potassium bismuth tartrate D. R. L. was accepted by the Council on Pharmacy and Chemistry for inclusion with New and Nonofficial Remedies and a description of the product published.[21]

### POWERS-WEIGHTMAN-ROSENGARTEN SPECIMEN

A specimen of potassium sodium bismuth tartrate was submitted to the Council on Pharmacy and Chemistry by Powers-Weightman-Rosengarten Company. This product as manufactured by Poulenc Freres of Paris, had been sold abroad under the name of "Luatol." The American manufacturers (P. W. R.) stated that the product was believed to have the composition represented by the formula

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[21] J. A. M. A. **82**: 209, 1924

$$[KNa(CO_2)_2]_3 \,.\, (CHOH)_4 \,.\, [CO_2(CHO)_2Bi]_2$$

The theoretical composition of this compound may be seen by an examination of Table 3. According to the submitted formula the product should contain no water of hydration. The product was a white, odorless powder, easily soluble in water to form a colorless solution having an alkaline reaction. Analysis of the salt by the methods previously described, omitting the treatment with ammonia water to produce solution, gave 8.74 per cent of potassium, 5.13 per cent of sodium, 31.41 per cent of bismuth and 12.53 per cent of loss on drying. The analysis shows that the product conforms reasonably closely with the theoretical formula if calculated as containing 9 molecules of water of hydration. A comparison of the findings and the theoretical formula is given in Table 3.

TABLE 3.—*Comparison of the P. W. R. Specimen of Potassium Sodium Bismutho-Tartrate with Theoretical Formulas*

| Theory for | Potassium | Sodium | siBmuth | Water of Hydration |
|---|---|---|---|---|
| $K_3Na_3Bi_2C_{16}H_{12}O_{24}$ .......... | 9.85 | 5.80 | 34.95 | 0 |
| $K_3Na_3Bi_2C_{16}H_{12}O_{24} + 9H_2O$.. | 8.67 | 5.10 | 30.75 | 11.98 |
| P. W. R. Specimen........... | 8.74 | 5.13 | 31.41 | 12.53 |

## TREPOL

Trepol is manufactured by Chenal, Douilhet & Co., of Paris. A specimen of Trepol in dry form was submitted to the Council on Pharmacy and Chemistry by the manufacturer's American agent, The Anglo-French Drug Co., of New York with the claim that it is "a tartro bismuthate of potassium and sodium containing 64 per cent of active bismuth." The formula claimed for the product is given herewith:

$$NaOOC-CHOH-CH(OBiO)-COOK \,.\, 4(BiO_2H)$$

A compound of the formula claimed should contain 74.4 per cent of bismuth, whereas the amount claimed by the manufacturer is "64 per cent of active bismuth." Since this formula contains but one tartrate radical, every bond of which is saturated without allowance for the four ($BiO_2H$) groups, the formula as submitted at first appeared untenable. The manufacturer explained that both of the acidic functions of the tartaric acid are blocked—one by potassium and the other by sodium. This combination is rendered insoluble by an excess of bismuth oxide so as to form a basic compound. This portion of the formula ($BiO_2H$) may be considered as bismuth hydroxide which has been partially dehydrated.

The specimen of Trepol examined was a pale yellowish white, finely granular, odorless powder. It was nearly insoluble in water, but soluble in acids with effervescense. On analysis, the preparation lost about 2.6 per cent by drying at 100°. No statement was made in the submission concerning the presence or absence of water of hydration. Determinations indicated about 72 per cent of bismuth[22] instead of 64 per cent as claimed. The product contained only about 1.3 per cent of potassium and only about 0.9 per cent of sodium instead of 2.79 per cent and 1.65 per cent respectively as is required by the formula submitted. Further, Trepol contained calcium, equivalent to 3.3 per cent of calcium carbonate. The presence of this substance was not declared in the submission and there appears to be no justification for its presence.

$$Bi_2S_3 \times 0.8122 = Bi$$

The analytical findings are tabulated herewith together with the composition as claimed by the formula:

TABLE 4.—*Analysis of Trepol Compared with the Composition Claimed*

| | Theory for Submitted Formula, Per Cent | Found, per Cent |
|---|---|---|
| Loss on drying | 0 | 2.59 |
| Bismuth | 74.44 | 72.10 |
| Potassium | 2.79 | 1.31 |
| Sodium | 1.65 | 0.89 |
| Calcium (equivalent to calcium carbonate) | 0 | 3.32 |

The findings for Trepol were brought to the attention of the manufacturer, who replied that the percentage of bismuth as found by the American Medical Association Laboratory was correct. While the theory of the formula required 74 per cent of bismuth, the manufacturer stated that the actual content may vary between 70 and 74 per cent, the average being from 72 to 73 per cent. The firm promised that the claim of 64 per cent of bismuth as made in the Trepol literature would be changed. The manufacturer claimed that not a trace of calcium could possibly be present in Trepol as none had been used in the manufacture of the product. The manufacturer also challenged the Laboratory's findings for potassium and sodium, claiming that the quantities as shown by the submitted formula were those actually present.

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[22] The method for the determination of bismuth which was found to give the best results is as follows: Weigh about 1 Gm. of the material, suspend it in 900 cc. of water, add 2 Gm. of potassium chloride, warm the mixture to 80° and saturate with hydrogen sulphide. Keep the mixture warm for three hours, passing in more hydrogen sulphide if necessary, collect the precipitate in a tared Gooch crucible, wash it, respectively, with water, alcohol, ether, carbon disulphide, alcohol and ether, dry to constant weight at 100° and weigh.

In view of the fact that the Laboratory findings had been challenged, a reexamination of the submitted specimen of Trepol was undertaken. The findings for the second analysis are given in Table 5.

TABLE 5.—*Second Analysis of Trepol*

| | |
|---|---|
| Loss on drying | 2.31 per cent |
| Bismuth | 72.69 per cent |
| Calcium | 1.51 per cent |
| Potassium | 1.63 per cent |
| Sodium | 0.86 per cent |
| Carbon dioxide ($CO_2$) | 4.79 per cent* |

* The specimen contained about 8 per cent of water-soluble material. This was found to consist almost entirely of potassium sodium tartrate.

From the results of the analysis it was calculated that the composition of the submitted specimen of Trepol was probably essentially as follows:

| | |
|---|---|
| Water of hydration | 2.3 per cent |
| Calcium carbonate | 3.7 per cent |
| Potassium sodium tartrate | 8.0 per cent |
| Bismuth subcarbonate (U. S. P. IX) | 36.7 per cent |
| Basic bismuth tartrate | 49.3 per cent |

In these calculations all of the calcium is assumed to be in combination with carbon-dioxide, and the balance of the carbon dioxide is assumed to be present in the form of bismuth subcarbonate having the approximate composition given in the U. S. Pharmacopeia. The balance of the bismuth is considered as a basic bismuth tartrate roughly approximating the composition claimed by Chenal, Douilhet & Co.

The findings for the second analysis of Trepol were submitted to the manufacturer. It was pointed out in the analytical report that the presence of calcium had been positively identified, notwithstanding the manufacturer's claim that not a trace of it could be present. The fact that the product contained nearly 5 per cent of carbon dioxide was mentioned and, as had been shown in the first analysis, the report emphasized further that the content of potassium and sodium was much lower than that indicated by the formula given by the manufacturer. The firm replied that their present analysis (made after the second report from the A. M. A. Chemical Laboratory had been received) confirmed the analysis of the A. M. A. chemists. They admitted the presence of calcium and of carbon dioxide but were unable to offer any satisfactory explanation for their presence.

The examination of Trepol reveals that its manufacturers, Chenal, Douilhet & Co., were ignorant of the composition of the product which they were selling. Its bismuth content was higher than claimed, it contained potassium sodium tartrate and calcium carbonate as impurities, and a considerable amount of other carbonate, probably bismuth subcarbonate, was present.

### METZ SPECIMEN

A specimen said to be potassium sodium bismuth tartrate was received from the H. A. Metz laboratories. This substance was not a market product, but its analysis was included as a matter of record. The manufacturer stated that the specimen contained 32 per cent of bismuth but that no determinations of potassium or of sodium had been made.

The product was a cream colored, hygroscopic powder, easily soluble in water forming a colorless solution which had an alkaline reaction to litmus. Determinations of bismuth, potassium, sodium and tartrate radicle were made. The analytical results are tabulated herewith:

Table 6.—*Analysis of the Metz Specimen*

| | |
|---|---|
| Bismuth | 34.09 per cent |
| Potassium | 0.59 per cent |
| Sodium | 15.31 per cent |
| Yield of tartaric acid | 44.22 per cent |

The great excess of sodium over potassium in the Metz specimen as compared with the Dermatalogical Research Laboratories specimen recorded earlier in this report, indicates that the product is not potassium sodium bismuth tartrate, but a sodium bismuth tartrate, containing small amounts of potassium salts.

### SPECIMENS FROM SYNTHETIC DRUG CO., LTD.

A specimen said to be potassium sodium bismuth tartrate (insoluble) and a specimen stated to be the soluble form of the first compound were submitted to the Council on Pharmacy and Chemistry by the Synthetic Drug Co., Ltd., of Toronto. The second product was stated by the manufacturers to have been prepared by dissolving the insoluble form in sodium hydroxide. The insoluble product was a white, bulky, odorless powder, practically insoluble in water. The aqueous suspension of the material was neutral to litmus paper. The soluble form was a white, odorless powder, soluble in water to form a clear, colorless solution which had an alkaline reaction to litmus. The products were analyzed and the findings are tabulated herewith:

TABLE 7.—*Analysis of Synthetic Drug Co. Specimens*

| Sample | Bismuth | Potassium | Sodium | Water of Hydration |
|---|---|---|---|---|
| Insoluble | 62.08 | 0.35 | 0.49 | 3.06 |
| Soluble | 57.06 | 0.35 | 6.38 | 1.78 |

From the results of the analysis it is evident that the first specimen is not a potassium sodium bismuth tartrate, but is probably a basic bismuth tartrate containing small amounts of potassium and sodium as impurities. The second specimen (soluble) is a sodium bismuth tartrate containing traces of potassium salts as impurities. When the analyiss was brought to the attention of the firm it accepted that its insoluble product was not a potassium sodium bismuth tartrate but was probably a bismuth tartrate and voluntarily decided to change the name.

### SUMMARY

The results of this examination reveal that there is considerable diversity in the composition of the bismuth tartrate compounds used in syphilotherapy. Some appear to be potassium sodium bismuth tartrate. These are relatively low in bismuth content, are soluble in water and their solutions have an alkaline reaction to litmus. Others are potassium bismuth tartrate. These also are relatively low in bismuth and are soluble in water. Still others appear to be sodium bismuth tartrate which contains small amounts of potassium salts. They are soluble in water to form solutions which are slightly alkaline to litmus. Their bismuth content is low. Others appear for the most part to be basic bismuth tartrates of unknown constitution but containing small amounts of sodium and potassium salts probably as impurities. Their bismuth content is relatively high and they are insoluble in water.

It is a reflection on manufacturing pharmacy that the error of Sazerac and Levaditi in calling the Cowley product potassium sodium bismuth tartrate has been allowed to remain in the literature for several years without challenge, whereas proper chemical control by the makers of Trepol would have revealed the error before any of the first batch of material had been marketed. The fact that some of these compounds have been used in so-called scientific research without their composition being known to the users is a reflection on research.

### Details of Analysis

#### Laboratory Specimen

*Loss or Gain in Weight on Exposure to Air.*—A weighed quantity of the salt which had been dried at 100 C. was exposed to the air for several days and the change in the weight noted. A sample weighing 1.5430 Gm. gained 0.036 Gm., equivalent to 2.33 per cent. A duplicate test was not carried out.

*Bismuth.*—Bismuth was first determined by an adaption of the method employed by Puckner and Hilpert in determining bismuth in bismuth beta-naphtholate (Am. Pharm. Assoc. Proc., **57,** 859, 1909). As applied to the Laboratory Specimen of bismuth tartrate it consisted in dissolving the specimen in about 0.1 per cent ammonia water, precipitating the bismuth as bismuth sulphide, dissolving the precipitate in nitric acid, filtering, evaporating somewhat and precipitating the bismuth as bismuth hydroxide by means of ammonia water and ammonium carbonate. The precipitate was collected in a weighed Gooch crucible, washed, dried, ignited, and weighed as bismuth oxide. This method was abandoned for a shorter one as follows:

> A weighed quantity of the bismuth salt was dissolved by agitation in about 0.1 per cent ammonia water, the bismuth precipitated as bismuth sulphide from the warm solution by hydrogen sulphide, the precipitate collected in a weighed Gooch crucible, washed successively with water, alcohol, ether, carbon disulphide, alcohol and ether in the order named, dried at 100 C. and weighed.

The findings for bismuth in the laboratory specimen are given herewith:

| Weight of Specimen, Gm. | Weight of $Bi_2S_3$, Gm. | Bismuth Equivalent, Gm. | Percentage of Bismuth |
|---|---|---|---|
| 1.1969 | 0.9112 | 0.7400 | 61.83 |
| 2.1009 | 1.5772 | 1.2810 | 60.97 |
| 1.8716 | 1.3975 | 1.1351 | 60.64 |

Average of three determinations, 61.14 per cent of bismuth.

*Tartaric Acid Liberated.*—Material weighing 10.0936 Gm. was dissolved in about 800 cc. of warm water by the aid of ammonia water, the bismuth precipitated by hydrogen sulphide and the filtrate treated by the following method:

> *Tartaric Acid.*—The filtrate from which the bismuth sulphide had been removed was slightly acidulated with hydrochloric acid, the solution evaporated to half its volume, the residue placed in a graduated 500 cc. flask and made up to volume with water. An aliquot portion of 100 cc. of the solution was evaporated to about 25 cc., an excess of potassium chloride added, followed by 2 cc. of glacial acetic acid and, after stirring, three volumes of alcohol with stirring. After standing overnight the precipitate (potassium bitartrate) was collected in a filter and washed with 50 per cent alcohol. The filter was then placed in a beaker containing hot water and the acidity titrated with normal sodium hydroxide, using phenolphthalein as indicator. The results were calculated to tartaric acid, $H_2C_4H_4O_6$. No correction was made for the potassium bitartrate soluble in the aqueous alcohol as the solubility is known to be small (Wenger, Am. Chem. Jour., **14**, 624, 1892; Roelofsen, Ibid., **16**, 466, 1894).

1 cc. N/1 NaOH = 0.1500 Gm. of $H_2C_4H_4O_6$

Of the diluted solution 100 cc. represents 2.0187 Gm. of original material.

| Weight Material, Gm. | Cc. of N/1 NaOH Consumed | Equivalent of Tartaric Acid | Percentage of Tartaric Acid Liberated |
|---|---|---|---|
| 2.0187 | 4.31 | 0.6467 | 32.0 |
| 2.0187 | 4.30 | 0.6421 | 31.9 |

The average for tartaric acid liberated was 31.95 per cent.

*Potassium and Sodium.*—An aliquot portion of the diluted filtrate from the bismuth determination was evaporated to dryness in the presence of an excess of sulphuric acid, the residue heated to low redness, cooled, a fragment of ammonium carbonate added and the residue again heated. The mixture of potassium sulphate and sodium sulphate was weighed, its sulphate content determined as barium sulphate in the usual way and the relative proportions of potassium and sodium calculated by the method described in the Annual Reports of the Chemical Laboratory, A. M. A., vol. 6, p. 44, 1913.

| Weight of Specimen, Gm. | Weight of Potassium Sodium Sulphate, Gm. | Weight of $BaSO_4$ | Equivalent of Sodium, Gm. | Percentage of Sodium | Equivalent of Potassium, Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| 5.0468 | 0.0914 | 0.1385 | 0.01716 | 0.34 | 0.01723 | 0.34 |
| 1.1969 | 0.0167 | 0.0304 | 0.00371 | 0.30 | 0.00244 | 0.22 |

Average 0.32 per cent of sodium and 0.28 per cent of potassium. Although the duplicates are not very close it was not considered worth while to make another determination because the quantities of sodium and potassium did not correspond anywhere near the values expected for a product having the composition $K_3Na_3Bi_2O_{16}H_{12}O_{24}$.

### DERMATOLOGICAL RESEARCH LABORATORY SPECIMEN

*Moisture.*—This was determined by drying a weighed quantity of the material at 100 C. to approximately constant weight.

| Weight of Specimen | Loss at 100 C. | Loss, per Cent | Average Loss, per Cent |
|---|---|---|---|
| 2.3128 Gm. | 0.1058 Gm. | 4.57 | 4.53 |
| 1.2516 Gm. | 0.0561 Gm. | 4.48 | .... |

*Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Bismuth Equivalent | Percentage of Bismuth | Average Bismuth, per Cent |
|---|---|---|---|---|
| 2.0925 | 1.6991 | 1.3801 | 65.95 | 65.73 |
| 1.1327 | 0.9138 | 0.7422 | 65.52 | ..... |

*Tartaric Acid Liberated*

| Weight of Specimen (from Aliquot) | Cc. N—1 NaOH Consumed | Equivalent of Tartaric Acid | Percentage of Tartaric Acid | Average Tartaric Acid |
|---|---|---|---|---|
| 1.02776 | 1.35 | 0.2086 Gm. | 20.3 | 20.5 |
| 2.56940 | 3.55 | 0.5327 Gm. | 20.7 | .... |

*Potassium*

| Weight of Specimen | Weight of $K_2SO_4$ | Equivalent of Potassium | Percentage of Potassium | Average per Cent of Potassium |
|---|---|---|---|---|
| 2.5694 Gm. | 0.3044 Gm. | 0.1365 Gm. | 5.32 | 5.26 |
| 2.0925 Gm. | 0.2121 Gm. | 0.1086 Gm. | 5.19 | .... |

### Powers, Weightman, Rosengarten Co. Specimen

*Loss on Drying at 100 C.*

| Weight of Sample | Loss at 100 C. | Percentage of Loss | Average of Loss per Cent |
|---|---|---|---|
| 1.1583 Gm. | 0.1449 Gm. | 12.51 | 12.53 |
| 2.0618 Gm. | 0.2588 Gm. | 12.55 | ..... |

*Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average of Bismuth |
|---|---|---|---|---|
| 1.5497 Gm. | 0.6009 Gm. | 0.4881 Gm. | 31.51 | 31.41 |
| 2.0167 Gm. | 0.7778 Gm. | 0.6316 Gm. | 31.31 | ..... |

*Sodium and Potassium*

| Weight of Specimen, Gm. | Weight of $Na_2SO_4$ + $K_2SO_4$, Gm. | Weight of $BaSO_4$, Gm. | Equivalent of Sodium (Average) Gm. | Percentage of Sodium (Average) | Equivalent of Potassium (Average) Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| 1.0084* | 0.3503 | 0.5194 | 0.0499 | 4.96 | 0.0904 | 8.96 |
| 1.0084* | 0.3580 | 0.5316 | ...... | .... | ...... | .... |
| 1.0084* | 0.3789 | 0.5180 | ...... | .... | ...... | .... |
| 1.5497 | 0.5517 | 0.8166 | 0.0833 | 5.31 | 0.1320 | 8.52 |

* Aliquots from solution.

Average 5.13 per cent of sodium and 8.74 per cent of potassium.

### Trepol (1st analysis)

*Loss on Drying at 100 C.*

| Weight of Specimen | Loss on Drying | Percentage of Loss | Average Loss |
|---|---|---|---|
| 1.1743 Gm. | 0.0311 Gm. | 2.65 | .... |
| 1.0342 Gm. | 0.0262 Gm. | 2.53 | 2.59 |

*Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average Bismuth |
|---|---|---|---|---|
| 1.0515 Gm. | 0.9343 Gm. | 0.7588 Gm. | 72.16 | ..... |
| 0.6376 Gm. | 0.5655 Gm. | 0.4593 Gm. | 72.03 | 72.10 |

In attempting to determine sodium and potassium it was discovered that the first determinations were valueless owing to the presence of calcium. This complicated the analysis.

Consequently the samples used for bismuth and tartaric acid (because of the addition of a potassium salt) could not be used for calcium, sodium and potassium. A weighed specimen (9.9141 Gm.) was dissolved in warm 1 per cent hydrochloric acid, the bismuth in the entire sample precipitated by hydrogen sulphide, the bismuth sulphide removed by filtration, the excess hydrogen sulphide removed from the filtrate by boiling, and the solution diluted to 1000 cc. Calcium was determined in 250 cc. portions of this dilution by the following method:

> The solution was evaporated to small volume to remove most of the excess of acid, the solution diluted with water to a bulk of about 75 cc. An excess of ammonium oxalate solution was added, the solution heated nearly to boiling and an excess of ammonium hydroxide added slowly. The mixture was kept hot for two hours and the bulk of the supernatant liquid decanted through a filter. The precipitate was dissolved in a slight excess of warm, dilute hydrochloric acid and the calcium reprecipitated in the usual way. The precipitate was collected in a weighed Gooch crucible, dried and ignited at a low temperature and weighed as calcium carbonate. The residue obtained in this way was moistened with ammonium carbonate solution, dried and the residue again heated and weighed.

| Weight of Specimen * | Weight of $CaCO_3$ | Equivalent of Calcium | Percentage of Calcium | Average per Cent of Calcium |
|---|---|---|---|---|
| 1.4785 Gm. | 0.0830 Gm. | 0.0332 Gm. | 1.34 | 1.33 |
| 2.4785 Gm. | 0.0816 Gm. | 0.0326 Gm | 1.32 | .... |

* From aliquot.

This is equivalent to 3.8 per cent of calcium carbonate.

*Sodium and Potassium.*—The filtrates from the calcium determination were used for the determination of sodium and potassium.

| Weight of Specimen,* Gm. | Weight of $Na_2SO_4$ + $K_2SO_4$, Gm. | Weight of $BaSO_4$, Gm. | Equivalent of Sodium, Gm. | Percentage of Sodium | Equivalent of Potassium, Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| 2.4785 | 0.1433 | 0.2128 | 0.0224 | 0.90 | 0.0333 | 1.34 |
| 2.4785 | 0.1381 | 0.2052 | 0.0217 | 0.87 | 0.0319 | 1.28 |

* From aliquot.

Average 0.89 per cent. of sodium and 1.32 per cent of potassium.

### TREPOL (2d analysis)

*Loss on drying at 100 C.*

| Weight of Specimen | Loss | Percentage of Loss | Average Loss |
|---|---|---|---|
| 1.1414 Gm. | 0.0263 Gm. | 2.30 | 2.31 |
| 1.1414 Gm. | 0.0266 Gm. | 2.32 | .... |

*Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average Bismuth |
|---|---|---|---|---|
| 1.3203 Gm. | 1.1829 Gm. | 0.9607 Gm. | 72.74 | 72.69 |
| 1.2747 Gm. | 1.1402 Gm. | 0.9261 Gm. | 72.65 | ..... |

*Calcium*

| Weight of Specimen | Weight of $CaCO_3$ | Equivalent of Calcium | Percentage of Calcium | Average Calcium |
|---|---|---|---|---|
| 1.3203 Gm. | 0.0475 Gm. | 0.0190 Gm. | 1.44 | 1.50 |
| 1.2747 Gm. | 0.0491 Gm. | 0.0190 Gm. | 1.55 | .... |

This is equivalent to 3.72 per cent of calucium carbonate.

*Sodium and Potassium*

| Weight of Specimen, Gm. | Weight of $K_2SO_4$ + $Na_2SO_4$, Gm. | Weight of $BaSO_4$, Gm. | Equivalent of Sodium, Gm. | Percentage of Sodium | Equivalent of Potassium, Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| 1.3203 | 0.0814 | 0.1192 | 0.0193 | 0.83 | 0.0214 | 1.62 |
| 1.2747 | 0.0820 | 0.1204 | 0.0114 | 0.89 | 0.0211 | 1.64 |

Average, 0.86 per cent of sodium and 1.63 per cent of potassium.

*Carbon Dioxide.*—This was determined by the Knorr method as described in the "Official and Tentative Methods of Analysis" of the A. O. A. C. ed. 1920, p. 277.

| Weight of Specimen | Weight of $CO_2$ | Percentage of $CO_2$ | Average $CO_2$ |
|---|---|---|---|
| 1.0404 Gm. | 0.0512 Gm. | 4.92 | 4.79 |
| 1.0560 Gm. | 0.0499 Gm. | 4.73 | .... |
| 1.06[illegible]8 Gm. | 0.0502 Gm. | 4.71 | .... |

*Potassium Sodium Tartrate.*—It was discovered that Trepol contained a noticeable amount of water-soluble material. Qualitative tests indicated that the water-soluble part contained potassium, sodium and tartrate. Accordingly some of the soluble material was obtained by percolating a known weight of the material (10.0985 gm.) with water, making the percolate to a volume of 500 cc. with water and assaying aliquot portions for total solids, tartaric acid liberated, sodium and potassium.

*Solids*

| Weight of Material (in Aliquot Portion) | Weight of Solids | Percentage of Solids | Average Solids |
|---|---|---|---|
| 2.0197 Gm. | 0.1648 Gm. | 8.20 | 8.17 |
| 2.0197 Gm. | 0.1636 Gm. | 8.15 | .... |

*Tartaric Acid Liberated*

| Weight of Material (in Aliquot Portion) | N—10 KOH Consumed | $NaKC_4H_4O_6$ Produced | Percentage of $NaKC_4H_4O_6$ |
|---|---|---|---|
| 3.0296 Gm. | 11.66 cc. | 0.2427 Gm. | 8.01 |
| 2.0197 Gm. | 7.70 cc. | 0.1618 Gm. | 8.01 |

*Analysis of the Insoluble Portion of Trepol.*—A weighed quantity of Trepol was treated with water; filtered after standing for several days, and the residue (or insoluble portion) dried in the air at ordinary temperature.

*Loss on Drying at 100 C.*

| Weight of Specimen | Loss in Weight | Percentage of Loss | Average Loss |
|---|---|---|---|
| 1.1617 Gm. | 0.0129 Gm. | 1.11 | 1.03 |
| 1.0582 Gm. | 0.0101 Gm. | 0.95 | .... |

*Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average Bismuth |
|---|---|---|---|---|
| 1.1617 Gm. | 1.1640 Gm. | 0.9454 Gm. | 81.38 | 81.30 |
| 1.0582 Gm. | 1.0358 Gm. | 0.8413 Gm. | 81.21 | ..... |

*Calcium*

| Weight of Specimen | Weight of $CaCO_3$ | Equivalent of Calcium | Percentage of Calcium | Average Calcium |
|---|---|---|---|---|
| 1.1617 Gm. | 0.0403 Gm. | 0.0161 Gm. | 1.39 | 1.45 |
| 1.0582 Gm. | 0.0399 Gm. | 0.0160 Gm. | 1.51 | .... |

*Potassium and Sodium.*—Determinations of these were not completed, as it was found that the total potassium sodium sulphate from the two specimens (2.2199 Gm.) weighed but 0.0092 Gm. This could not amount to more than 0.2 per cent of total potassium and sodium.

### CONCLUSION

The analysis shows that the water-washed specimen of Trepol contains about 1 per cent of moisture, 81 per cent of bismuth and nearly 1.5 per cent of calcium. The total quantities of potassium and sodium are less than 0.2 per cent. A comparison of the analysis of the water-washed specimen of Trepol with the analysis of the unwashed specimen is given in the accompanying table.

| | First Analysis | Second Analysis | Washed Specimen |
|---|---|---|---|
| Loss at 100 C. | 2.59 | 2.31 | 1.03 |
| Bismuth | 72.10 | 72.69 | 81.30 |
| Calcium | 1.33 | 1.50 | 1.45 |
| Potassium | 1.31 | 1.63 | Less than 0.20 |
| Sodium | 0.89 | 0.86 | |

## H. A. METZ LABORATORIES SPECIMEN

*Loss on Drying at 100 C.*—The specimen was received in a sealed tube. It proved to be very hygroscopic so that no determinations of moisture were made.

### *Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average Bismuth |
|---|---|---|---|---|
| 1.0227 Gm. | 0.4341 Gm. | 0.3526 Gm. | 34.47 | ..... |
| 1.0489 Gm. | 0.4420 Gm. | 0.3590 Gm. | 34.22 | ..... |
| 0.7899 Gm. | 0.3295 Gm. | 0.2676 Gm. | 33.87 | 34.09 |
| 0.9515 Gm. | 0.3960 Gm. | 0.3216 Gm. | 33.80 | ..... |

### *Sodium and Potassium*

| Weight of Specimen, Gm. | Weight of $NaKSO_4$, Gm. | Weight of $BaSO_4$, Gm. | Equivalent of Sodium, Gm. | Percentage of Sodium | Equivalent of Potassium, Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| 0.7899 | 0.3876 | 0.6283 | 0.1363 | 15.38 | 0.0042 | 0.53 |
| 0.9515 | 0.4642 | 0.7572 | 0.1450 | 15.23 | 0.0162 | 0.66 |

Average, 15.31 per cent of sodium and 0.59 per cent of potassium.

### *Yield of Tartaric Acid*

| Weight of Specimen | N/10 NaOH Consumed | Equivalent of Tartaric Acid | Percentage of Tartaric Acid | Average Tartaric Acid |
|---|---|---|---|---|
| 1.1941 Gm. | 35.12 cc. | 0.5270 Gm. | 44.13 | 44.22 |
| 1.0314 Gm. | 30.46 cc. | 0.4571 Gm. | 44.31 | ..... |

## SPECIMENS FROM SYNTHETIC DRUG CO.

### *Loss on Drying at 100 C.*

| Weight of Specimen | Loss in Weight | Percentage of Loss | Average Loss |
|---|---|---|---|
| Insoluble | | | |
| 1.0541 Gm. | 0.0309 Gm. | 2.93 | 3.06 |
| 1.0263 Gm. | 0.0319 Gm. | 3.18 | .... |
| Soluble | | | |
| 1.0945 Gm. | 0.0051 Gm. (gain) | .... | .... |
| 1.0217 Gm. | 0.0182 Gm. (loss) | 1.78 | 1.78 |

### *Bismuth*

| Weight of Specimen | Weight of $Bi_2S_3$ | Equivalent of Bismuth | Percentage of Bismuth | Average Bismuth |
|---|---|---|---|---|
| Insoluble | | | | |
| 1.0047 Gm. | 0.7681 Gm. | 0.6248 Gm. | 62.19 | 62.08 |
| 1.0057 Gm. | 0.7673 Gm. | 0.6232 Gm. | 61.96 | ..... |
| Soluble | | | | |
| 1.0945 Gm. | 0.7647 Gm. | 0.6222 Gm. | 56.74 | ..... |
| 1.0217 Gm. | 0.7251 Gm. | 0.5889 Gm. | 57.64 | 57.06 |
| 1.4957 Gm. | 1.0456 Gm. | 0.8499 Gm. | 56.90 | ..... |
| 0.5263 Gm. | 0.4170 Gm. | 0.2999 Gm. | 56.93 | ..... |

### *Sodium and Potassium*

| Weight of Specimen, Gm. | Weight of $NaKSO_4$, Gm. | Weight of $BaSO_4$, Gm. | Equivalent of Sodium, Gm. | Percentage of Sodium | Equivalent of Potassium, Gm. | Percentage of Potassium |
|---|---|---|---|---|---|---|
| Insoluble | | | | | | |
| 1.0541 | 0.0272 | 0.0401 | 0.0061 | 0.58 | 0.0031 | 0.30 |
| 1.0263 | 0.0229 | 0.0345 | 0.0042 | 0.40 | 0.0041 | 0.40 |
| Soluble | | | | | | |
| 1.4957 | 0.3047 | 0.4968 | 0.0967 | 6.46 | 0.0022 | 0.15 |
| 1.0217 | 0.2082 | 0.3380 | 0.0633 | 6.20 | 0.0057 | 0.55 |

Average, 0.49 per cent of sodium and 0.35 per cent of potassium for the insoluble form and 6.33 per cent of sodium and 0.35 per cent of potassium from the soluble form.

# A QUALITATIVE TEST TO SHOW THE ABSENCE OF CITRATE OR TARTRATE IN MIXTURES[1]

*(Reprinted from Industrial and Engineering Chemistry, Vol. 17, No. 11, page 1146. November, 1925)*

**By Joel B. Peterson, Ph.D.**

CHICAGO

The tests for the presence of tartrates and citrates are well known. When the tests are negative, however, there is often doubt as to their reliability. In other words, it is often difficult to indicate tartrates or citrates when these are present in small amounts and are mixed with other substances.

Incidental to some work undertaken in this laboratory, it was found possible to demonstrate the absence of even small amounts of citrates and tartrates. It was observed that extremely small amounts of these compounds interfere with the beautiful purple color of the ferric salicylate complex. Presumably the change of color is due to the repression of the ferric ion by the tartrate or citrate ion.

## SOLUTIONS

The solutions used were those described in New and Nonofficial Remedies, 1925,[2] page 319, for testing for salicylates in acetylsalicylic acid. They were prepared as follows:

*Sodium Salicylate.*—Dissolve 0.116 gram sodium salicylate in distilled water and dilute to 1000 cc.

*Ferric Chloride Solution.*—To 1 cc. of ferric chloride reagent U. S. P., add 50 cc. of water. Add ammonia water, U. S. P., drop by drop and shake after each addition. Sufficient has been added when the precipitate which forms dissolves only after vigorous shaking. Add 1 drop of glacial acetic acid and dilute the solution to 100 cc. with water. (This solution should be prepared fresh every day.)

## TEST

In each of two colorimetric tubes put 25 cc. of water, 1 cc. of alcohol,[3] 1 cc. of the sodium salicylate, and 1 cc. of the ferric chloride solution. Add the citrate, tartrate, or unknown solution to one tube and dilute both to exactly 50 cc. and shake until the solutions are well mixed. A portion of citric acid weighing 0.0002 gram, or 0.0006 gram of caffein citrate, or 0.0003 gram of potassium bitartrate gives an opalescence quite readily recognizable when the solution is compared with the similarly made up control tube. A larger portion of citrate or tartrate discharges the violet color completely, leaving a yellow color.

---

[1] Received July 6, 1925.

[2] Published by the Council on Pharmacy and Chemistry of the American Medical Association.

[3] The alcohol is used in case a water-insoluble, alcohol-soluble unknown is used. In this case the unknown can be dissolved in alcohol and the other solutions added to it.

It is probable that other aliphatic hydroxy acid radicals will act similarly.

## CONCLUSIONS

1. The absence of citrate as caffeine citrate in amounts not less than 1 part in 80,000, of citric acid in amounts not less than 1 part in 250,000, and of potassium bitartrate in amounts not less than 1 part in 125,000 can be tested by the foregoing procedure.

2. A change in the color of the ferric salicylate complex when present in the strength described in this paper can be observed by the addition of citrate, tartrate, or any other substance capable of repressing the ferric ion.

3. The test is probably of most value in confirming the absence of small amounts of citrates and tartrates. It is particularly applicable to the analysis of medicinal mixtures.

# PART II

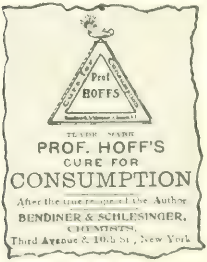
## REPORTS BASED ON ARTICLES WHICH APPEARED IN THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION AND IN HYGEIA

### CITROPHAN

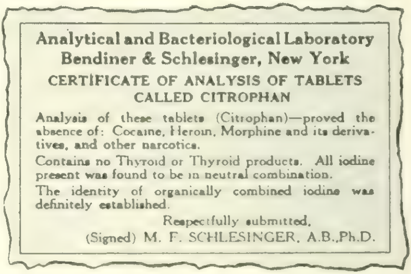
### Another "Fat Cure" Nostrum Exploited to the Medical Profession and the Public

*(Abstracted, with additions, from The Journal A. M. A., March 1, 1924, p. 734)*

"Citrophan" is one of the latest "patent medicines" to be exploited to the obese. It is put on the market by the Gotham Corporation which does business from New York City. This concern was incorporated in Delaware in February, 1922, and is nominally located with the United States Corporation Company at Dover, Delaware.


Prof
HOFFS
Cure for Consumption

TRADE MARK
PROF. HOFF'S
CURE FOR
CONSUMPTION
After the true recipe of the Author
BENDINER & SCHLESINGER,
CHEMISTS,
Third Avenue & 10th St., New York



**Analytical and Bacteriological Laboratory**
**Bendiner & Schlesinger, New York**
**CERTIFICATE OF ANALYSIS OF TABLETS CALLED CITROPHAN**

Analysis of these tablets (Citrophan)—proved the absence of: Cocaine, Heroin, Morphine and its derivatives, and other narcotics.

Contains no Thyroid or Thyroid products. All iodine present was found to be in neutral combination.

The identity of organically combined iodine was definitely established.

Respectfully submitted,
(Signed) M. F. SCHLESINGER, A.B.,Ph.D.

On the right is a photographic reproduction (reduced) of the "Certificate of Analysis" testimonial used by the Citrophan people, and coming from Bendiner & Schlesinger. On the left is a photographic reproduction (reduced) of "Prof. Hoff's Cure for Consumption," also put out by Bendiner & Schlesinger. When the federal Food and Drugs Act made lying on the label illegal, "Prof. Hoff's Cure for Consumption" became "Prof. Hoff's Prescription."

The nostrum is advertised and sold to the public on the mail-order plan. An elaborate colored circular, illustrated pamphlets and the inevitable batch of testimonials are being used in their exploitation.

### WHAT IS CITROPHAN?

The claims made for "Citrophan" are many and various. Back of them all is a fundamental thesis developed by the exploiters and expressed in the advertising, thus:

> "Science has found that the chief cause of obesity lies in the *development of alcohol in the digestive tract,* brought about by the action of *yeast bacteria*—taken into the stomach in improperly baked bread—and on raw fruit and vegetables."

Here it may be said that this basic claim is utterly unsupported by scientific work. There are many types of obesity and there are undetermined causative factors in all of them but science has *not* found that the chief cause of obesity is due to the development of alcohol in the digestive tract. As the foundation is false, naturally the superstructure is essentially unsound. Here are some specific claims:

> "The Citrophan treatment has the endorsement of chemists, physicians, professors of leading universities and medical colleges. . . ."
>
> "With only three little Citrophan tablets daily, you may lose 10, 20 and even 30 pounds a month. . . ."
>
> "This wonderful discovery called Citrophan is the result of worldwide study of the perplexing problem of obesity. It is not the work of a day or a month, but of years of research and practical experiment."
>
> "Users of Citrophan often lose several pounds of flesh a week, and sometimes as much as a pound or more a day."
>
> "This wonderful product has been endorsed by medical authorities and the leading chemists of America as absolutely harmless and phenomenally effective."
>
> "Just as modeling-clay is moulded into beautiful form beneath the deft fingers of a sculptor's hand, so will burdensome fat melt away under the gentle action of Citrophan — *revealing the Venus underneath your fat.*"

Those who are on the "sucker list" of the Gotham Corporation first receive a form letter signed "H. H. Rubin, M.D., Medical Director." It is in this letter that Rubin brags of his "extended [*sic!*] practice" and his "broad experience." Accompanying it are two order blanks, one for forty-two Citrophan tablets, for which $4.00 is asked, and the other for one hundred and sixty-eight Citrophan tablets, price $12.50. Those who order receive a small package containing the Citrophan tablets and also a small batch of laxative tablets called "Fangerine." The instructions are, take two Citrophan tablets three times a day and one or two Fangerine tablets each night. As is the case with all "obesity cure" nostrums, the purchaser is told (after she has spent her money) that, to get good results, it is necessary to "avoid eating foods made of white flour as well as sweets"; also one must not eat potatoes or bananas.

Orders for the Citrophan treatment were sent in from different localities, these were then subjected to examination in the chemical laboratory.

*Citrophan.*—This product is sold in the form of brown tablets in tubes. Each tube contains 21 tablets. The tablets in some of the packages had a noticeable odor like oil of peppermint. Others did not have this odor. The average weight of the tablets in different packages varied from about 4½ grains (0.3040 Gm.) to more than 7 grains (0.4592 Gm.).

Qualitative tests indicated the absence of alkaloids, free iodine, water-soluble iodides, benzoates, salicylates, and the purgative salts, such as magnesium sulphate and potassium sodium tartrate. Neither could tetraiodopyrrol (iodol), a substance which has been employed in another alleged obesity cure, be found. The chief medicinal constituent of the tablets appeared to be tetraiodophenolphthalein. Sugar of milk (lactose) also was present in considerable quantities. Smaller amounts of starch, vegetable tissue and traces of an acid-insoluble substance (probably talc) were found. Traces of iron and phosphates were found in the ash. By shaking some of the powdered tablets with petroleum benzin, about 2 per cent. of an organic substance was removed which was not identified. It seems probable that this substance, together with the starch, talc and vegetable tissue is used merely as a binder to hold the ingredients together.

From the results of the quantitative examination it is concluded that the composition of Citrophan is essentially as follows:

| | |
|---|---|
| Tetraiodophenolphthalein ................ | 40 per cent. |
| Lactose (sugar of milk).................. | 52 per cent. |
| Ash (including talc).................... | 3 per cent. |
| Starch and undetermined................ | 5 per cent. |

About twenty-five years ago tetraiodophenolphthalein, the chief medicinal ingredient of Citrophan, was exploited in Europe under the name "Nosophen" as an external and internal antiseptic and substitute for iodoform. The product, while on the American market has never attracted much attention in this country.

In circulars advocating the use of Citrophan, which are distributed by the Gotham Corporation, the statement is made that Citrophan contains a recently discovered organic iodine compound derived from bone-oil which is stated to be insoluble in an acid or an alkaline medium or in alcohol. As a matter of fact, tetraiodophenolphthalein has been known for about thirty years and is soluble in alcohol and in alkaline solutions.

*Fangerine.*—This comes in the form of gray-brown tablets, each package containing eighteen tablets. The tablets have an odor like chocolate and a sweet, chocolate-like taste. The weight of the tablets is about 0.9 Gm. each, or nearly 14 grains. Qualitative tests indicate the presence of chocolate, sugar (sucrose) and phenolphthalein. No other medicinal substances were found. Quantitative determinations indicated that Fangerine contained about 50 per cent. of sugar and about 11 per cent. of phenolphthalein or about 1.5 grains of phenolphthalein in each tablet.

In concluding the article, THE JOURNAL stated: Evidently, therefore, "Citrophan," instead of being a wonderful new discovery, is a resurrection, under another name, of a drug that has been used for a third of a century—tetraiodophenolphthalein, which is also sold under the proprietary name "Nosophen."

## Details of Analysis

*Petroleum Benzin Soluble.*—Some of the tablets were powdered in a mortar as finely as conveniently possible and the powder passed through a No. 40 sieve as completely as possible. The coarser particles were then returned to the mortar and ground until they could be passed through the sieve. The whole of the powder was then thoroughly mixed. A weighed quantity of the powder was then washed successively by decantation with small amounts of petroleum benzin, the solvent decanted through a filter, the filtrate evaporated to dryness, the residue dried over sulphuric acid and weighed. From 1.6889 Gm. of material 0.0362 Gm. of petroleum benzin soluble material was obtained, equivalent to 2.14 per cent. A duplicate of 6.4876 Gm. gave 0.0968 Gm. of petroleum benzin soluble material, equivalent to 1.49 per cent. A third weighing of 18.3684 Gm. from another lot of tablets gave 0.5009 Gm. of petroleum benzin soluble material, equivalent to 2.727 per cent; average of three determinations, 2.11 per cent of petroleum benzin soluble material in the tablets. This substance, after recrystallization from petroleum benzin, melted at 83-85 C., although the melting point was not very sharp. It was insoluble in water but soluble in alcohol, chloroform and ether. Tests indicated that it did not contain either iodine or nitrogen. It did not respond to tests for alkaloids, cincophen, alphanaphthol, betanaphthol, phenolphthalein, guaiacol carbonate, guaiacol benzoate, benzoic acid, succinic acid, naphthalene or phenol.

*Tetraiodophenolphthalein.*—A weighed quantity of the powdered tablets (which had previously been washed with petroleum benzin) was placed in a Gooch crucible, the powder covered with a small mass of purified cotton and the powder extracted with benzene in a Soxhlet apparatus for 30 hours. The benzene solution was evaporated, the residue dried at 60 C. and weighed. The extract from 0.4252 Gm. (equivalent to 0.4345 Gm. of original material) weighed 0.1720 Gm., equivalent to 39.58 per cent. Another weight (from a different lot of tablets) of 1.2722 Gm. (equivalent to 1.3078 Gm. of original material) gave 0.4820 Gm. or 36.94 per cent. Average, 38.26 per cent. Portions of this residue gave a violet-blue color on treatment with sodium hydroxide solution and a rose-red color with sulphuric acid. By treatment with sodium hydroxide, potassium permanganate, nitric acid, sulphur dioxide and silver nitrate as described by Seeker and Mathewson (Bur. Chem. Circ. 65) an abundance of silver iodide was obtained. Some of the extract gave off purple vapors when ignited in a porcelain crucible. A particle of the extract gave a dirty violet color on treatment with sulphuric acid and potassium ferrocyanide.

*Lactose.*—Lactose was determined as follows: The residue remaining after the benzene extraction was dried at 100 C. to remove the excess of solvent and the residue extracted with water in a Soxhlet apparatus. The water extract was clarified in the usual way, by the addition of lead acetate solution. The mixture was made up to 100 cc. The mixture was filtered through a dry filter and 50 cc. of the filtrate treated with an excess of sodium sulphate solution. The mixture was filtered and the solution made up to 100 cc. After standing over night to overcome birotation, a portion of this solution was placed in the polariscope and the optical rotation observed with sodium light. Portions of the solution obtained from 0.4252 Gm. of material (equivalent to 0.4345 Gm. of the original) gave a rotation of 0.23° and 0.24° in a 200 mm. tube, or an average of 0.235°. This is equivalent to 52.79 per cent of lactose. A duplicate from 0.3372 Gm. of material (equivalent to 0.34457 Gm. of original material) gave a rotation of 0.19°, equivalent to 0.18147 Gm. of lactose or 52.66 per cent. Average, 52.72 per cent of lactose.

*Starch.*—Some of the residue remaining after successive extractions with benzene and water was examined under the microscope both without and in the presence of a trace of free iodine. Before adding iodine solution, small particles were seen which were taken to be starch grains. After adding iodin solution these became blue.

*Talc.*—The powder, as examined under "starch" in the preceding paragraph, showed fine, shining, irregular shaped particles resembling particles of talcum examined as a control. The ash of the whole tablet material contained similar particles which were insoluble in hydrochloric acid.

*Iron.*—A weighed portion of the powdered tablet material was heated to redness, the cooled residue moistened with water, dried and again heated. This treatment was repeated until the residue ceased to lose weight. 1.0414 Gm. of material (equivalent to 1.0765 Gm. of original material) yielded 0.0334 Gm. of ash or 3.12 per cent. The ash was treated with hydrochloric acid and the solution filtered. The filtrate gave a red color when treated with potassium sulphocyanate solution.

*Phosphate.*—A portion of the acid-soluble ash gave a yellow precipitate on the addition of ammonium molybdate solution.

### FANGERINE

The weight of ten tablets was taken. The average weight of the tablets was 0.9023 Gm. or about 13.92 grains.

*Phenolphthalein.*—A weighed portion of the tablets was extracted with petroleum benzin in a Soxhlet apparatus to remove fats and the solvent discarded. The residue was then extracted with acetone, the solvent evaporated, the residue moistened with alcohol, dried at 100 C. and weighed. From 1.1193 Gm. of material a residue of 0.1229 Gm. was obtained, equivalent to 10.98 per cent. This is equivalent to about 1.5 grains of phenolphthalein for each tablet.

*Sucrose.*—The residue remaining from the acetone extraction was extracted with water and the solution made up to 100 cc. The optical rotation of this solution was observed in a 100 mm. tube. The observed rotation was 0.36°. This is equivalent to 48.81 per cent of sucrose.

## HAIR DYES

*(This report was the basis of an article, "To Dye or Not to Dye," by Dr. Arthur J. Cramp, which appeared in Hygeia, July, 1924, p. 449.)*

A number of hair dyes were examined for toxic constituents by qualitative tests. The preparations tested were:

Mrs. S. A. Allen's World's Hair Color Restorer; Barbo Compound; Kolor-Bak; La Creole Hair Dressing; Q-Ban Hair Color Restorer; Wyeth's Sage & Sulphur; Eau Sublime (two solutions); Inecto Rapid (two solutions); Mrs. Potter's Walnut Juice Hair Stain (two solutions); Farr's Gray Hair Restorer; and Mary T. Goldman's Gray Hair Color Restorer

Each of these preparations had been examined previously, either in this laboratory or by chemists connected with various State and Municipal Laboratories, and the findings published. Hence the only tests applied in this examination were such as were necessary to determine whether the preparations contained the same poison as had been found previously. The results found in the laboratory are tabulated together with the findings previously reported:

| | Found | Previously Reported |
|---|---|---|
| Mrs. S. A. Allen's World's Hair Color Restorer | Lead Acetate<br>Sulphur | Lead Acetate<br>Glycerin<br>Sulphur |
| Barbo Compound | Lead Acetate<br>Chloride<br>Sulphate<br>Sulphur | Lead Acetate<br>Sulphur<br>Sodium Sulphate |
| Kolor-Bak | Lead Acetate<br>Sulphur<br>Chloride | Lead Acetate<br>Lead Chloride<br>Sulphur |
| LaCreole Hair Dressing | Lead Acetate<br>Sulphur | Lead Acetate<br>Sulphur<br>Glycerin<br>Alcohol |
| Q-Ban Hair Color Restorer | Lead Acetate<br>Sulphur | Lead Acetate<br>Sulphur<br>Glycerin<br>Alcohol |
| Wyeth's Sage and Sulphur | Lead Acetate<br>Sulphur | Lead Acetate<br>Sulphur<br>Glycerin<br>Capsicum |
| Eau Sublime A | Paraphenylenediamine<br>Ammonia | Paraphenylenediamine |
| B | Hydrogen Peroxide | Hydrogen Peroxide |
| Inecto Rapid A | Paraphenylenediame or some related compound | Paraphenylenediamine |
| B | Hydrogen Peroxide | Hydrogen Peroxide |
| Mrs. Potter's Walnut Tint Hair Stain (1) | Paraphenylenediamine | Paraphenylenediamine |
| (2) | Hydrogen Peroxide | Hydrogen Peroxide |
| Farr's Gray Hair Restorer | Silver salt in an alkaline solution | Ammoniacal Solution of Silver Nitrate |
| Mary T. Goldman's Gray Hair Color (1) | Silver salt in an alkaline solution | Weak Ammoniacal Solution of Silver Nitrate |
| (2) | Sodium Thiosulphate | |

The Goldman product now comes in two packages—one a liquid and the other solid. The latter, which appears to be partially dried sodium thiosulphate, apparently has not been reported previously.

The examination of these eleven hair dyes reveals that the composition, at least so far as concerns the presence of toxic constituents, is essentially the same as that previously reported. Each contains a poisonous ingredient, apparently in considerable amounts.

*Paraphenylenediamine.*—This dye was tested for by each of the tests given below. In each instance except that of Inecto the test was positive and satisfactory. When applied to Inecto the tests did not respond well. From the results it was concluded that Inecto probably contained paraphenylenediamine or some closely related substance with some other substances which interfered with the tests to some extent.

Some of the liquid was mixed with an equal volume of hydrogen peroxide solution and the mixture placed on paper or cotton. This became bluish-black on drying.

A splinter of pine wood was dipped into the liquid and then treated with dilute acetic acid. The wood became bright red.

A drop of the liquid was placed on a white surface and then treated with a drop of bromine water. The mixture became at first a bright green and then a dull violet color.

## SUN AND MOON OIL AND OINTMENT

### The Quackeries of A. W. Lowrie of Hartford, Conn.

*(Abstracted, with additions, from The Journal A. M. A., Aug. 9, 1924, p. 458)*

Alfred W. Lowrie, an alleged "divine healer," does business, or did if he does not still, at Hartford, Connecticut. Lowrie mixes religion with his quackery. According to the Hartford *Courant*, many prominent Hartford people place some reliance in Lowrie's quackeries. In addition to his work as a "healer," Lowrie has also made some excursions into literary fields, to say nothing of his activities as a "patent medicine" manufacturer.

Lowrie, it seems, has published his interpretations of "Visions of Life." In this he is said to have claimed that he died once and while dead was ushered into the presence of the Supreme Being. While in heaven Lowrie was presented with the "Key to Knowledge," with the understanding that this knowledge was to be used by him when he returned to earth through spiritual, magnetic and electric powers which would be conferred on him on his return to this mundane sphere.

After Lowrie's visit to the Divine Presence he seems to have started making what he is pleased to call "Sun and Moon Sacred Ointment" and "Sun and Moon Sacred Anointing Oil."

### THE SACRED OINTMENT

According to the little tin box in which it comes, Sun and Moon Sacred Ointment "contains vibrations of life from the radio-activity of electricity, magnetism, electrons and atoms." The purchaser is advised to "put ointment on fingers, anoint and manipulate it into the body and you will receive strength and vitality." In addition we read, still from the trade package:

> "If you are a sufferer of any part of the body anoint with this ointment which is filled with atoms and vibations of life. For internal use take the size of a pea a number of times a day. It acts as a tonic. Snuff up nostrils to clear the head.
>
> "QUICK RELIEF Catarrh, Colds, Croup, Sore Throat, Influenza, Growths, Neuritis, Sciatica, Rheumatism, Neuralgia, Piles, Sores, Sun Burn, Burns, Blood Pressure, Hardening of Arteries and Nerves, Etc."

The Laboratory was asked to analyze the Sun and Moon Sacred Ointment and obtained original, unopened specimens for that purpose.

SUN AND MOON SACRED OINTMENT.—The material was a greenish ointment having a strong odor of oil of wintergreen and a less noticeable odor of oil of sassafras. On heating a portion of the ointment on a water bath, the material melted and finally left a brownish yellow residue which in the melted form had the greenish fluorescence and otherwise physical characteristics of petrolatum. This residue amounted to 92.7 per cent of the original material. It contained a noticeable amount of fine insoluble particles which under the microscope were seen to be similar to coal dust and street "dirt." On cooling, the liquefied, oily, nonvolatile residue solidified to a brownish yellow mass of ointment like consistency. Analysis indicated that about 18 per cent of this residue consisted of a saponifiable fat, and the balance of an unsaponifiable substance having the properties of petrolatum. Zinc oxide, lead plaster, soap, alkaloids, iodides and extractives from capsicum or ginger were absent. Quantitative analysis indicated that the composition of Sun and Moon Sacred Ointment is essentially as follows:

| | |
|---|---|
| Petrolatum | 75.50 per cent. |
| Saponifiable fat | 17.20 per cent. |
| Methyl salicylate | 4.00 per cent. |
| "Dirt" | 0.15 per cent. |
| Oil of sassafras, water and undetermined | 3.15 per cent. |

Should any one wish to make a preparation having the essential physical properties of Sun and Moon Sacred Ointment and yet not wish to undergo the harrowing experience of dying for the purpose of getting the information, the product may be made as follows: Melt together 80 parts of lubricating grease (such as "cup grease"), 15 parts of suet, 4 parts of oil of wintergreen, one part of oil of sassafras, a sprinkling of street dirt, and stir until cool.

### THE SACRED OIL

Unopened original specimens of Sun and Moon Sacred Anointing Oil were also obtained by the Laboratory. The bottle label stated that the preparation was both for external and internal use. "For weariness and pain, also after bathing, anoint the body with Sun and Moon Anointing Oils." Furthermore, the public was told that the product had "no equal for tired and sore feet, rheumatism, neuritis, lameness, hardening of the arteries and nerves, stiff joints and cords, broken bones, sore muscles, bruises, burns, growths, skin diseases, toothache, backache, chapped hands, sun burn." Whether it would cure smallpox, measles, soft corns or hardening of the liver was not stated; however, if one wanted "to regulate bowels and kidneys," he was instructed "to anoint bowels and back." Also, one-quarter teaspoonful taken internally twice a day was a splendid thing "for colds, stomach, liver or intestinal trouble, and tired exhausted nerves." And, too, the preparation "acts as a food for the body."

The Laboratory subjected this sacred preparation to a profane analysis.

SUN AND MOON SACRED ANOINTING OIL. This came in 3½-ounce, panel bottles, corked and sealed with wax. The preparation appeared to consist for the most part of a pale yellow oil together with a small amount of a brownish liquid at the bottom of the bottle. On shaking, the mixture emulsified, but on standing the brownish liquid separated and settled to the bottom of the container again. No information concerning the composition of the Sun and Moon Sacred Anointing Oil was given by the manufacturer except that 3 per cent of alcohol was declared on the label. The preparation had a pronounced odor like oil of wintergreen and a less noticeable odor like oil of sassafras. The reaction toward moistened litmus paper was very faintly acid. Qualitative tests indicated the absence of sulphates, benzoic acid, oil of turpentine, extractives from capsicum or ginger, alkaloids, purgative salts, emodin-bearing (laxative) drugs and ammonium compounds. A fixed oil was found in large amounts. This had the properties (specific gravity, iodine number and saponification number) of olive oil. Methyl salicylate (oil of wintergreen) was also present in considerable amounts. Small quantities of a vegetable extractive which had no distinctive properties, oil of sassafras and traces of chlorides were indicated. The ash was insignificant. The vegetable extractive, which was very small in amount, contained no potent ingredients. The quantitative determinations gave the following results:

| | |
|---|---|
| Specific gravity at $\frac{25\ C.}{25\ C.}$ | 0.92571 |
| Loss on drying at 100 C. | 13.43 per cent. |
| Residue on drying at 100 C. | 86.57 per cent. |
| Fixed oil (having the properties of olive oil) | 85.61 per cent. |
| Methyl salicylate (oil of wintergreen) | 4.25 per cent. |
| Alcohol | 1.23 per cent.* |
| Water, oil of sassafras and vegetable extractive. | 8.91 per cent.† |

The foregoing determinations indicate that Sun and Moon Sacred Anointing Oil consists essentially of fixed oil (probably olive oil) 87 parts, methyl salicylate 5 parts, oil of sassafras 1 part, alcohol 2 parts, water and vegetable extractive 5 parts.

Again, for those who would like to experiment in making a "sacred" product, a preparation having essentially the same properties as Sun and Moon Sacred Anointing Oil may be made by mixing:

| | |
|---|---|
| Olive oil | 87 parts |
| Artificial oil of wintergreen | 5 parts |
| Oil of sassafras | 1 part |
| Tincture of arnica | 5 parts |
| Water | 2 parts |

---

* By weight.

† Difference.

## Details of Analysis

### Sun and Moon Sacred Annointing Oil

*Specific Gravity.*—As the specimen was not a homogeneous mixture the specific gravity could not be taken accurately. The material was shaken in order to produce an emulsion and the specific gravity of the emulsion taken with a pycnometer. By this approximate method the specific gravity was found to be 0.92 at 25C./25C.

*Residue on Drying.*—A weighed quantity of the well shaken material was dried at 100 C. to approximately constant weight. From 3.7279 Gm. of material a residue of 3.2279 Gm. was obtained, equivalent to 86.58 per cent. A duplicate of 4.0831 Gm. gave 3.5344 Gm. of residue, equivalent to 86.56 per cent. Average, 86.57 per cent.

*Olive Oil.*—A measured volume of the well shaken material was distilled with steam, the cooled, non-volatile residue shaken with ether, the solvent evaporated, the residue dried at 80 C. and weighed. From 50 cc. of the material (46.2855 Gm.) the weight of non-volatile oil amounted to 38.4392 Gm., equivalent to 83.05 per cent. From 100 cc. (92.5710 Gm.) a weight of 81.5853 Gm. of oil was obtained, equivalent to 87.9 per cent. Average, 85.5 per cent. The specific gravity of this oil was found to be 0.9128 at 25 C. and 0.919 at 15 C.

The iodine absorption number and saponification number of this oil were taken by the methods described in Official and Tentative Methods of Analysis of the A. O. A. C. 1920, pp. 244 and 246. The results were compared with the constants for eleven of the more common fixed oils used in medicine or which are found in commerce. The comparison may be seen by reference to Table 1. The constants given are taken as far as possible from the U. S. P. IX. The constants for the oils not described in the U. S. P. IX. and certain constants not mentioned by the U. S. P. IX. are taken either from Leach's Food Inspection and Analysis, ed. 4, 1920, as revised by Winton, or from Analyze der Fette und Wachsarten by Benedikt und Ulzer, 1908.

*Methyl Salicylate.*—A measured volume of the well mixed material was steam distilled until the odor of methyl salicylate was no longer detected and a few drops of the distillate in 5 cc. of water no longer gave a violet color with a ferric chloride solution. The entire distillate was mixed with an equal volume of alcohol, 20 Gm. of potassium hydroxide dissolved in the mixture and the solution boiled in a reflux apparatus

### TABLE 1

| Oil | Specific Gravity at $\frac{25\text{ C.}}{25\text{ C.}}$ | Specific Gravity at $\frac{15\text{ C.}}{15\text{ C.}}$ | Iodine No. (Hanus) | Saponification Number | Index of Refraction at 25 C. |
|---|---|---|---|---|---|
| Almond | 0.910 | 0.915 | 93-100 | 191-200 | 1.4710 to 1.4715 (at 20 C.) |
| Castor | 0.945 | 0.965 | 83-88 | 179-185 | 1.4783 to 1.4789 (at 20 C.) |
| Cod liver | 0.918 | 0.922 | 140-180 | 180-190 | 1.4783 to 1.4822 |
| Cotton seed | 0.915 | 0.921 | 105-114 | 190-198 | 1.4698 to 1.4723 |
| Croton | 0.935 | 0.950 | 104-110 | 200-215 | 1.4757 to 1.4768 |
| Lard (oil) | 0.915<br>at $\frac{15.5\text{ C.}}{15.5\text{ C.}}$ | 0.918 | 67-88 | 190-198 | 1.4620 to 1.4660 |
| Linseed | 0.925 | 0.935 | 170-187 | 187-195 | 1.4789 to 1.4824 |
| Olive | 0.910 | 0.915 | 79-90 | 190-195 | 1.4659 to 1.4685 |
| Peanut | 0.917<br>at $\frac{15.5\text{ C.}}{15.5\text{ C.}}$ | 0.926 | 83-105 | 186-196 | 1.4691 to 1.4707 |
| Rape | 0.913<br>at $\frac{15.5\text{ C.}}{15.5\text{ C.}}$ | 0.917 | 94-105 | 168-179 | 1.4708 to 1.4723 |
| Sesame | 0.916 | 0.921 | 103-112 | 188-193 | 1.4710 to 1.4723 |
| Unknown | 0.9128 | 0.91926 | 84.57<br>85.01<br>85.31 | 192.16<br>192.80<br>...... | 1.4682<br>......<br>...... |

for 2 hours. The alcohol was then removed by distillation and the residual solution diluted to 1000 cc. Aliquot portions were acidified with diluted sulphuric acid and the solution shaken out thrice with ether. The ether solutions were united, the mixture washed with water and the ether solution evaporated to dryness. The residue of salicylic acid was dried over sulphuric acid and weighed.

$$C_6H_4(OH)COOH \times 1.1015 = C_6H_4(OH)COOCH_3$$

The distillate from 50 cc. of the preparation (46.2855 Gm.) was finally brought to a volume of 1000 cc. The salicylic acid from 50 cc. of this solution weighed 0.0888 Gm., equivalent to 4.23 per cent of methyl salicylate in the original mixture. A duplicate of 100 cc. gave 0.1798 Gm. of salicylic acid, equivalent to 4.27 per cent of methyl salicylate. Average 4.25 per cent of methyl salicylate.

*Alcohol.*—Alcohol was determined by the method described in the U. S. P. IX for substances containing volatile oils (U. S. P. IX, p. 592). The distillate from 100 cc. was finally brought to 100 cc. The specific gravity of this distillate at $\frac{15.6C}{15.6C}$ was 0.99766, equivalent to 1.56 per cent of alcohol by volume.

*Oil of Sassafras.*—The odor of the original preparation and the odors obtained at various stages of the analysis suggested oil of sassafras. Since the quantity present was believed to be small, no attempt was made to determine it, or to separate it from the methyl salicylate present.

### Sun and Moon Sacred Ointment

*Residue on Drying.*—A weighed portion of the ointment was dried to approximately constant weight on the steam bath. The residue from 4.0441 Gm. of material weighed 3.7505 Gm., equivalent to 92.74 per cent. A duplicate of 2.8994 Gm. yielded a residue of 2.6855 Gm., equivalent to 92.62 per cent. Average, 92.68 per cent of residue.

*"Dirt."*—A weighed portion of the material was dissolved in warm carbon tetrachloride, the solution filtered through a weighed Gooch crucible, the insoluble residue washed with carbon tetrachloride, dried at 100 C. and weighed. From 15.0780 Gm. of material, an insoluble residue of 0.0217 Gm. was obtained, equivalent to 0.14 per cent. A duplicate determination was not carried out. Under the microscope the

particles of insoluble material resembled coal dust and other miscellaneous objects such as are found in street dirt.

*Methyl Salicylate.*—This was determined by the same method as is described under Sun and Moon Sacred Annointing Oil. From 2.7056 Gm. of material 0.0776 Gm. of salicylic acid was obtained, equivalent to 3.16 per cent of methyl salicylate. A duplicate of 2.6176 Gm. gave 0.0994 Gm. of salicylic acid, equivalent to 4.18 per cent of methyl salicylate. Average, 3.66 per cent of methyl salicylate. During some processes of the analysis the odor of oil of sassafras was quite distinctly noticeable.

*Non-Volatile Material.*—A weighed sample of the original was evaporated to approximate constant weight on the steam bath. The residue was boiled in a reflux apparatus for two hours with alcoholic potassium hydroxide. The alcohol was removed by evaporation and the cooled residue extracted several times with ether. The ether solutions were washed with water, the solvent evaporated, the residue dried and weighed as "unsaponifiable substance." The residue of soap remaining in the separator after the removal of the unsaponifiable matter was acidified with dilute sulphuric acid, the mixture shaken repeatedly with small portions of ether, the solvent bulked the mixture washed with water, the solvent evaporated, the residue dried at 100 C. and weighed as "fatty acids from the saponifiable fraction."

*Unsaponifiable.*—From 1.1726 Gm. of the material 0.9093 Gm. of unsaponifiable material remained, or 77.55 per cent. From 25.4790 Gm. of the material 18.6064 Gm. of unsaponifiable residue was obtained, equivalent to 73.02 per cent. Average, 75.29 per cent of unsaponifiable. The unsaponifiable portion was fluorescent when melted and possessed other characteristics of petrolatum (such as color and consistency) of that quality which is used as a lubricant.

*Fatty Acids.*—The fatty acids from 1.1726 Gm. of the material amounted to 0.1681 Gm., equivalent to 14.33 per cent. The acids from 25.4790 Gm. of material amounted to 4.5421 Gm., or 17.82 per cent of free acid. This was multiplied by the factor 1.07 fatty acid to convert to "tallow."

*Iodine Number of the Fatty Acids.*—The iodine number of the free fatty acids was determined by the Hanus method as described in the Official and Tentative Methods of Analysis of the A. O. A. C., 1920, p. 244. The iodine number was found to be 38.9. The acid number of the fatty acids was determined by the official method for free fatty acids (Ibid. p. 250) but using a smaller quantity than there specified. The acid number found was 202.6. The melting point of the fatty acid lay between 46 and 47 C. According to various authors quoted by Benedikt and Ulzer (Analyze der Fette und Wachsarten, 1908) the iodine number of mutton tallow varies from 30.96 to 46.2, most of the value lying around 37 to 39 and the iodine number of the fatty acids from mutton tallow is about 35. The melting point of the fatty acids (from mutton tallow) is from 45 to 47 and the saponification number about 210. From the findings for the unknown substance it was concluded that the saponifiable part of the non-volatile portion of the Sun and Moon Sacred Ointment consists essentially of tallow. The constants were not sufficiently narrow to judge whether this had been obtained from the sheep or from the ox although the evidence pointed to the sheep.

A comparison of the constants found with those given in the literature showed that all of the oils except castor, lard, olive and peanut are eliminated by the iodine number alone. Of these the saponification number and specific gravity eliminated castor oil. The identification then lay between the oils from lard, olive and peanut. The refractive indexes of the several oils as given in the literature indicates pretty clearly that the oil is from the olive and not from the peanut.

## BIOFOOD

### A Worthless Nostrum Exploited Under Pernicious Claims

*(Abstracted, with additions, from The Journal A. M. A., Sept. 6, 1924, p. 782)*

"BioFood" is a "patent medicine" combination put out by a concern that seems to go under various names: "Biochemical Food Products Corporation," "Bio-Products Company" and "BioFood Corporation." The Biochemical Food Products Corporation was incorporated in Illinois, Oct. 7, 1920. The incorporators are given as Eugen Kuhne, S. Ashley Guthrie and Benj. H. Weisbrod, the two latter being lawyers. On Aug. 30, 1922, the name was changed to BioFood Corporation.

BioFood has been shrewdly and cleverly marketed. The psychic claptrap of the "patent medicine" faker has been used to good advantage. The name itself, "BioFood," may be counted on to disarm the newspaper publisher who might bar from his pages "patent medicine" advertisements. The impression is given that the stuff is a "food," and not a medicine. The physical layout is equally clever. BioFood is sold at a high price—$10.00 a "treatment"—which in itself can be counted on to impress the public with its value. The "treatment" consists of a box labeled "A" and two bottles labeled, respectively, "B" and "C." "BioFood A" consists of large tablets, resembling in general appearance the tablets of malted milk put up by various manufacturers. "BioFood B" also consists of tablets but smaller in size. "BioFood C" is a 5-ounce bottle of a dark brown liquid with an aromatic odor. "BioFood A" is claimed to contain "Sodium, Calcium, Iron, Manganese, Silicon, Carbon, Potassium, Magnesium, Lactophosphates, Glycerophosphates, With Lactose, Cocoa, and Charcoal as Filler." "BioFood B" is labeled as containing "a combination of chemicals among which are sodium, citrate, sulphate, lithium glycerophosphate and potassium sulphate." "BioFood C," the liquid, according to the label, "contains, among other ingredients, ammonium carbonate, magnesium glycerophosphate, iron glycerophosphate, calcium, sodium and manganese." As no quantities are given on any of the labels the alleged formulas are obviously meaningless.

BIOFOOD
"A"
BIOCHEMICAL FOOD PRODUCTS CORP.
BIOFOOD
"C"
BIOCHEMICAL FOOD PRODUCTS CORP.
BIOFOOD
"B"

The BioFood "Treatment" price $10.00, not worth 10 cents.

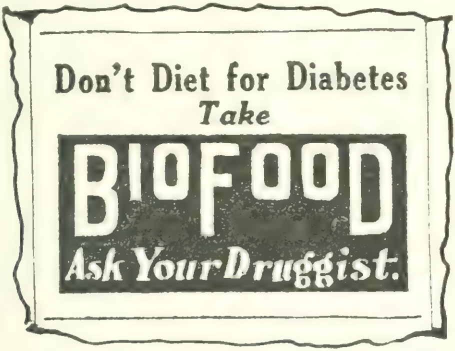
### THE BIOFOOD THEORY

In the exploitation of BioFood a thesis is put forward that reminds one of the dictums on which cults are founded; in fact, the BioFood exploiters seem to use as a basis the fantastic theory of Schussler and his so-called bio-chemic treatment by means of "twelve tissue remedies." The BioFood theory may be briefly stated thus:

(1) Our bodies are composed of twelve tissues containing sixteen elements.

(2) The same sixteen elements are found in virgin soil which has not been subjected to intensive cultivation.

(3) The soil today, because of intensive cultivation and the use of commercial fertilizer is deficient in many of these elements, therefore, our foods are deficient in the elements necessary to keep our bodies fit. Furthermore, we still further devitalize foods in preparing them for consumption.



**Don't Diet for Diabetes**
*Take*
**BIOFOOD**
*Ask Your Druggist.*

One of the viciously cruel slogans of the BioFood fakery. This advertisement ran in newspapers and street cars.

(4) BioFood contains all the elements in which modern soil and food is deficient and thus "builds up the body by supplying all the elements which nature intended man to have and thus gives nature a chance to create her own antitoxins and effect a cure."

This, then, is the theory on which the exploitation of BioFood is based. The claim that, because of soil deficiency, the natural foods of today are lacking in certain essential elements necessary to health has no foundation in fact. It is true—in fact a platitude—that some of our *prepared* foods are overrefined and "devitalized." But the idea of overcoming the deficiency of certain elements in overrefined foods, by taking pills, powders or liquids alleged to contain the deficient elements is unsound and absurd.

### SOME PERNICIOUS ADVICE

The BioFood advertising campaign has been extensive—full-page advertisements in newspapers, half-page advertisements in prostituted self-styled medical journals and cruelly mendacious advertisements in the Chicago street cars. Of the latter there is one reading:

### "DON'T DIET FOR DIABETES, TAKE BIOFOOD"

Whether the heartless disregard for human life expressed in this advertisement is the result of crass ignorance on the part of the BioFood concern or something worse makes little difference so far as its effect on the public is concerned. In addition to the display advertisements an elaborate follow-up series has been used to catch the potential victims that might answer some of the BioFood advertising.

A complete "treatment" of BioFood—price $10.00—was purchased by the Laboratory for analysis, although it was not expected that anything the laboratory might find would make BioFood seem any more preposterous than it was made to seem by the claims put forth.

### LABORATORY FINDINGS

One box of "BioFood," distributed by the Biochemical Food Products Corporation, Chicago, was purchased from a local druggist, price $10.00. The box, a relatively large size, contained three smaller packages, labeled "BioFood A," "BioFood B" and "BioFood C," respectively.

The following quantitative estimates were made:

**BioFood A.**—The box of "BioFood A" contained ninety tablets, each tablet occupying an individual cache in a "sanitape package." According to the label, "BioFood A" contains:

> "Sodium, Calcium, Iron, Manganese, Silicon, Carbon, Potassium, Magnesium, Lactophosphates, Glycerophosphates with Lactose, Cocoa, and Charcoal as Filler. Free from Alcohol and Narcotics. Not habit-forming."

The average weight of the tablets was 1.65 Gm. (about 25 grains). Qualitative tests confirmed the presence of the metallic elements claimed; tests were also positive for phosphate ($PO_4$), sugar, fat, and small amounts of chloride, sulphate and carbonate. Alkaloids, iodides, and emodin-bearing (laxative) drugs were not found. Silicon, of course, could not be present as such, but there was present a large amount of substance insoluble when digested with sulphuric and nitric acids, having the properties of magnesium silicate (talc).

From the qualitative and quantitative analyses made "BioFood A" may be considered to be composed essentially of milk sugar and flavoring in which has been incorporated small amounts of iron, calcium and manganese salts; and

| | | |
|---|---|---|
| Ash | 21.6 | per cent. |
| Water soluble material | 73.8 | per cent. |
| Material insoluble in acid (talc) | 11.7 | per cent. |
| Moisture (loss in weight at 120 C for 4 hours) | 8.4 | per cent. |
| Iron ($Fe^{+++}$) | 1.0 | per cent. |
| Manganese ($Mn^{++}$) | 0.11 | per cent. |
| Calcium ($Ca^{++}$) | 0.98 | per cent. |
| Magnesium (other than insoluble residue) | 0.00 | per cent. |
| Phosphate (as $PO_4^{\equiv}$) | 2.06 | per cent. |
| Lactose | 61.8 | per cent. |

phosphate, either as such or in combination such as glycerophosphates. The amount of iron in one tablet would be 0.016 Gm. (¼ grain), the amount of manganese 0.002 Gm. (1/30 grain) and calcium .016 Gm. (¼ grain) and talc 0.2 Gm. (3 grains).

BioFood B.—The bottle of "BioFood B" contained thirty-one white tablets. According to the label:

> "BioFood B contains a combination of chemicals, among which are sodium, citrate, sulphate, lithium glycerophosphates and potassium sulphate. These are the salts found in the most beneficial mineral springs. BioFood B is not a physic."

Each tablet weighed approximately 0.75 Gm. (about 11½ grs.). Qualitative tests indicated the presence of sodium, potassium, acetate, chlorid and citrate. Phosphate and lithium were not found by use of delicate tests although the presence of these radicals is declared on the label. Quantitative determination yielded the following:

| | | |
|---|---|---|
| Moisture (loss in weight 2½ hours at 150 C.) | 11.65 | per cent. |
| Water insoluble material (starch, etc.), of which 6.4% was acid insoluble (talc.) | 12.8 | per cent. |
| Sodium ($Na^{+}$) | 21.15 | per cent. |
| Potassium ($K^{+}$) | 6.41 | per cent. |
| Chlorid ($Cl^{-}$) | 15.21 | per cent. |
| Sulphate ($SO_4^{=}$) | 17.2 | per cent. |
| Acetate ($CH_3COO$) | 9.2 | per cent. |
| Citrate $C_6H_4O_7^{=}$) (calculated from excess sodium) | 8.2 | per cent. |

Calculating from the quantitative analysis made "BioFood B" may be considered to consist essentially of:

| | |
|---|---|
| Potassium acetate | 15 parts |
| Sodium chlorid | 25 parts |
| Sodium sulphate | 25 parts |
| Sodium citrate (anhydrous)<br>(Equivalent to 13.8 U. S. P.) | 11 parts |
| Moisture | 11 parts |
| Excipient | 13 parts |
| | 100 parts |

For each tablet, this would be equivalent to potassium acetate 0.11 Gm. (1.7 grains); sodium chloride 0.19 Gm. (2.9 grains); sodium sulphate 0.19 Gm. (2.9 grains) and sodium citrate U. S. P. 0.10 Gm. (1.5 grains).

BIOFOOD C.—The bottle of "BioFood C" contained about 150 cc. (5 fluid ounces) of a dark brown liquid having an aromatic odor. According to the label:

> "BioFood C contains among other ingredients, ammonium carbonate, magnesium glycerophosphate, iron glycerophosphate, calcium, sodium and manganese. Free from alcohol and narcotics. Not habit-forming."

Qualitative tests indicated the presence of acetate, phosphate, trace of sulphate, trace of chloride, calcium, iron, sodium and ammonium ($NH_4^+$). Sugar, alkaloids, iodides, manganese and carbonate were not found although the latter two are declared to be present, according to the label. Tests also indicated the presence of glycerin. The solution was acid to litmus. Quantitative estimates yielded the following:

| | |
|---|---|
| Specific Gravity | 1.089 |
| Loss in weight at 100 C for 18 hours | 75.9 per cent. |
| Ash | 2.2 per cent. |
| Calcium ($Ca^{++}$) | 0.20 per cent. |
| Iron ($Fe^{+++}$) | 1.01 per cent. |
| Magnesium ($Ng^{++}$) | 0.07 per cent. |
| Sodium ($Na^+$) | |
| Phosphate ($PO_4^{\equiv}$) | 0.12 per cent. |
| Acetate ($CH_3COO^-$) | 5.49 per cent. |
| Ammonium ($NH_4^+$) | 0.68 per cent. |

From the foregoing it is evident that "BioFood C" resembles Solution of Iron and Ammonium Acetate U. S. P. (Basham's Solution), modified by the addition of very small amounts of calcium, magnesium and sodium and phosphate compounds. The label claims the presence of ammonium carbonate and extols the virtue due to this product. Obviously ammonium carbonate "the anti-acid for various gastric disturbances" cannot be present as the product contains free acetic acid.

In commenting on this nostrum, THE JOURNAL stated:

> "How long will this piece of quackery continue? Just so long as the BioFood Company has money to spend on advertising and newspapers and street car companies are willing to share in the profits of quackery by accepting such advertising. The BioFood concern is merely one of many patent medicine exploiters that attempt to capitalize the present interest in the newer findings in food studies. The forward-looking nostrum maker of today knows that his public can be more easily humbugged on the 'food tonic' scheme than by any other. All that is necessary is an extensive and intensive advertising campaign written in a plausible and apparently, conservative tone. The well-to-do and more intelligent part of the public is particularly impressed by a scheme of this kind.
>
> "Newspapers that would turn down advertising contracts for 'Lydia Pinkham's' or 'Peruna' willingly publish advertisements of such pieces of quackery as 'BioFood' represents. Thus does the 'patent medicine' business adjust itself to changing conditions and the ever gullible public rise to new bait."

## Details of Analysis

### BIOFOOD "A"

The tablets were powdered in a mortar, and this powdered material used for the determination.

*Ash.*—The material was placed in a porcelain evaporating dish and heated to dull redness. 4.6512 Gm. yielded 1.0048 Gm. of ash, equivalent to 21.6 per cent.

*Solubility in Water.*—The material was treated with 250 c.c. of water, shaken and filtered. 5.0234 Gm. left a residue weighing 1.3276 Gm., equivalent to 26.2 per cent.

*Moisture.*—A sample weighing 1.7257 Gm. was dried in an oven at 120 C. for four hours. The loss in weight was 0.1449 Gm., equivalent to 8.4 per cent.

*Acid-Insoluble Material and Iron.*—A sample weighing 5.2326 Gm. was digested with sulphuric acid with aid of a small amount of nitric acid until all carbon compounds had been oxidized. The acid solution was diluted and filtered through a tared Gooch crucible in such a manner that the filtrate was saved quantitatively. The weight of the dry material was

0.6182 Gm., equivalent to 11.6 per cent. This material was fused with sodium carbonate; the fused mass was found to contain magnesium, aluminum and silica. It was concluded that the material was talc.

The filtrate was made up to exactly 500 c.c., and aliquot portions used for the iron determinations. To 50 c.c. of the solution, 5 c.c. of sulphuric acid was added and solution evaporated and heated until copious evolution of fumes occurred. The solution was diluted, the ferric sulphate reduced with hydrogen sulphide to ferrous sulphate, being kept saturated for two hours. The hydrogen sulphide was removed by passing hydrogen through the solution, finally under heat (the stoppered flask was heated on a hot plate and hydrogen [plus any removed hydrogen sulphide] conducted away some distance by means of tubing). The solution was then titrated with tenth-normal potassium permanganate. (a) 50 c.c. required 1.0 c.c. tenth normal potassium permanganate, equivalent to 1.06 per cent. of iron ($Fe^{++}$ or $Fe^{+++}$). (b) 50 c.c. required 0.95 c.c. of tenth normal potassium permanganate, equivalent to 1.01 per cent.

*Manganese.*—A sample weighing 4.1207 Gm. was treated with boiling concentrated nitric acid in a Kjeldahl flask, for six hours, diluted, filtered and with washings made up to 500 c.c. An aliquot portion was evaporated with 5 c.c. of sulphuric acid until acid fumes appeared (to remove nitric acid) diluted with 75 c.c. of water and the manganese precipitated by addition of 9 Gm. of ammonium persulphate in 75 c.c. of water according to the method of G. v. Knorre (see Analytic Chemistry, Treadwell and Hall, 5th edition, p. 620). The solution was heated to boiling, 100 c.c. more of water added and kept at boiling temperature for twenty minutes. The precipitate was filtered off, washed, and dissolved in excess (10 c.c.) of standardized ferrous sulphate solution (10 Gm. of $FeSO_4.7H_2O$; 50 c.c. of $H_2SO_4$ and 950 c.c. of $H_2O$). The excess of standardized ferrous sulphate was titrated with tenth normal potassium permanganate. (a) The amount of tenth normal (calculated) ferrous sulphate oxidized by the precipitate from 100 c.c. aliquot sample was 0.3 c.c., equivalent to 0.10 per cent. manganese ($Mn^{++}$). (b) The second titration was 0.4 c.c., equivalent to 0.13 per cent. manganese.

*Calcium.*—A sample weighing 2.3500 Gm. was boiled vigorously with nitric acid in a Kjeldahl flask for three hours, diluted with 125-150 c.c. of water, filtered and made up to 500 c.c. An aliquot portion was made slightly ammoniacal, then made acid with citric acid, heated to boiling, an excess of ammonium oxalate added and allowed to stand 72 hours. The precipitate was filtered, washed, transferred to tared platinum crucible, ignited in blast flame to calcium oxide and weighed. This method separating the calcium from iron was suggested by the procedure used by Puckner and Warren in the Analysis of calcium glycerophosphate (Jour. Am. Pharm. Assoc., July 1912, p. 749); (Ann. Rept. A. M. A. Chemical Laboratory 1912, Vol. 5, page 12.) A solution containing ferric chloride and sodium phosphate and citric acid gave no precipitate on addition of ammonium oxalate; with calcium chlorid a copious precipitate formed. (a) A 50 c.c. aliquot yielded 0.0030 Gm. Calcium oxide, equivalent to 0.91 per cent. calcium ($Ca^{++}$). (b) A 150 c.c. aliquot yielded 0.0118 Gm. calcium oxide, equivalent to 1.05 per cent. calcium.

*Phosphate.*—A sample, weighing 4.2102 Gm. was boiled vigorously with concentrated nitric acid for 1 hour, diluted, filtered (amount of insoluble material 0.4957 Gm., equivalent to 11.77 per cent.) and the filtrate made up to exactly 500 c.c. An aliquot was treated with ammonium molybdate as usuel at 70 C. three hours, then allowed to stand 24 hours. The precipitated phosphomolybdeum compound was filtered off and washed with water containing ammonium nitrate and nitric acid. The precipitate (still in the funnel) was treated with ammonia water until all had dissolved, and the filter paper washed well. To the combined filtrate and washings, magnesia mixture was then added, the mixture allowed to stand for eighteen hours; the magnesium ammonium phosphate filtered, ignited and weighed as $Mg_2P_4O_7$. (a) Fifty c.c. yielded 0.0052 Gm. magnesium pyrophosphate, equivalent to 2.10 per cent phosphate ($PO_4^{\equiv}$). (b) One hundred c.c. yielded 0.0100 Gm. of magnesium pyrophosphate, equivalent to 2.03 per cent phosphate ($PO_4^{\equiv}$).

### BioFood "B"

Some of the tablets were powdered, the powder well mixed and used for the quantitative determinations.

*Moisture.*—Because of presence of citrate and acetate, the loss in weight was determined at 150 C. for two and one-half hours. A sample weighing 0.7266 Gm. lost in weight 0.0843 Gm., equivalent to 11.6 per cent.

*Water-Insoluble Material.*—A sample weighing 0.8360 Gm. was shaken with water in a glass stopper Erlenmeyer flask for a period of one-half hour. The insoluble residue was filtered, weighed, on counterpoised filter and dried at 120 C. for two hours. The weight of the residue was 0.0107 Gm. equivalent to 12.8 per cent. (a large portion was starch and substance resembling talc).

*Acid-Insoluble Material.*—A sample weighing 5.2090 Gm. was boiled vigorously in a Kjeldahl flask for three hours, the insoluble material (resembling talc) filtered through a tared Gooch funnel and the filtrate made up to 500 c.c. The insoluble material weighed, after drying and washing, 0.3348 Gm., equivalent to 6.4 per cent. The filtrate was used for sodium and potassium, and sulphate determination.

*Sodium and Potassium.*—An aliquot was treated with sulphuric acid, evaporated, heated with free flame until converted to normal sulphates and weighed. The potassium was determined by weighing platinum, as described in Annual Reports A. M. A. Chemical Laboratory Volume 8, page 53. (a) Twenty-five c.c. yielded 0.2079 Gm. of combined sulphates and 0.0420 Gm. of platinum. This is equivalent to 21.09 per cent. sodium, and 6.64 per cent. potassium. (b) Twenty-five c.c. yielded 0.2091 Gm. combined sulphates and 0.0410 Gm. platinum, equivalent to 21.21 per cent. sodium and 6.65 per cent. potassium.

*Sulphate.*—An aliquot was diluted with 200 c.c. of water, acidified with hydrochloric acid, heated to boiling and an excess of hot barium chloride added. The beaker containing the mixture was placed on steam bath for two hours, then the precipitate filtered on tared Gooch crucible and washed well with hot water. (a) Fifty c.c. yielded 0.2165 Gm. barium sulphate, equivalent to 17.1 per cent sulphate ($SO_4^{=}$). (b) Fifty c.c. yielded 0.2184 Gm. barium sulphate, equivalent to 17.2 per cent sulphate ($SO_4^{=}$).

*Chloride.*—The solution from the solubility determination was made up to 250 c.c., and aliquot used to determine chloride according to the usual silver chloride method. (a) Fifty c.c. yielded 0.1029 Gm. silver chloride, equivalent to 15.21 per cent (b) Fifty c.c. yielded 1.1029 Gm., equivalent to 15.21 per cent.

*Volatile Acid (Acetic).*—The characteristic odor of acetic acid was noticeable on acidification of some of the sample; also ethyl acetate odor was obtained after appropriate treatment. A weighed sample of the material was suspended in 5 c.c. of water in a steam distillation apparatus (for illustration see Methods of Analysis [1919] A. O. A. C. page 177). An excess of tartaric acid added and the distillate titrated with tenth normal sodium hydroxide. (a) Fifty c.c. required 8.0 c.c.

of tenth normal sodium hydroxide, equivalent to 9.11 per cent acetate ($CH_3COO^-$). (b) Fifty c.c. required 8.5 c.c. of tenth normal sodium hydroxide, equivalent to 9.3 per cent. acetate ($CH_3COO^-$).

*Citric Acid and Calculations.*—The amount of acetate and potassium were approximately in equimolecular proportions, hence in the hypothetical combination potassium acetate was considered present. The sulphate and chloride were calculated to sodium and the excess sodium then calculated to citrate. The citrate radical responded to the Deniges tests as described under the Analysis of Sal Hepatica (Annual Reports A. M. A. Chemical Laboratory Volume 14, 1921, page 49) except that a larger amount of potassium permanganate was used than is suggested in the description given.

### BioFood "C"

*Residue and Ash.*—Twenty c.c. was pipetted in an evaporating dish, placed on water bath and finally in oven at 100 C. for 18 hours. The residue weighed 5.3487 Gm., equivalent to 24.1 per cent. The dish containing the material was carefully ignited, leaving an ash weighing 0.4831 Gm., equivalent to 2.2 per cent.

*SOLUTION "A".*—Solution "A" was used for quantitative determinations. It was composed of 50 c.c. of the original made up to 500 c.c.

*Iron.*—An aliquot of "A" was boiled for a few minutes with nitric acid, evaporated to dryness, taken up with small amount of hydrochloric acid, and tartaric acid added, and saturated for some hours with hydrogen sulphide, the precipitate filtered off, dissolved, in hydrochloric acid, ammonium chloride added and made ammoniacal. The precipitate ferric hydroxide was converted to the oxide and weighed. (a) Fifty c.c. yielded 0.078 Gm. of ferric oxide, equivalent to 1.01 per cent. iron ($Fe^{++}$ or $Fe^{+++}$). (b) Fifty c.c. yielded 0.078 Gm. of ferric oxide, equivalent to 1.01 per cent. iron ($Fe^{++}$ or $Fe^{+++}$).

*Calcium.*—To an aliquot of "A," a few c.c. of hydrochloric acid was added, heated, then added an excess of ferric chloride. Then added ammonium hydroxide until permanent precipitate formed, then just sufficient hydrochloric acid to dissolve it. The solution was then treated with ammonium acetate to remove both the ferric phosphate and excess iron according to usual treatment. The precipitate was filtered off, ammonium oxalate added and precipitated calcium oxalation filtered off, washed and converted to calcium oxide by aid of a blast lamp.

The filtrate was used for determination of magnesium. (a) Twenty-five c.c. of "A" yielded 0.0057 Gm. calcium oxide, equivalent to 0.14 per cent. calcium ($Ca^{++}$). (b) Twenty-five c.c. yielded 0.0097 Gm. calcium oxalate, equivalent to 0.25 per cent. calcium ($Ca^{++}$).

*Phosphate.*—Phosphate was determined according to method given under BioFood "A." (a) Fifty c.c. of "A" yielded 0.0081 Gm. of magnesium pyrophosphate, equivalent to 0.12 per cent.

*Magnesium.*—Magnesium was determined in the filtrate from calcium by precipitation with sodium phosphate. (a) Weight of magnesium pyrophosphate was 0.0180 Gm., equivalent to 0.072 per cent. magnesium ($Mg^{++}$). (b) Weight of magnesium pyrophosphate was 0.0165 Gm., equivalent to 0.066 per cent magnesium.

*Ammonium ($NH_4^+$).* (a) (Five c.c. of the original was treated with sodium hydroxide and steam passed through as described under acetic acid in "B," the end of condenser connected with an adapter which was immersed in 25 c.c. half normal hydrochloric acid, the excess titrated with half normal alkali. The amount of acid consumed was 2.02 c.c., equivalent to 0.67 per cent. ammonium ($NH_4^+$). (b) The amount of acid consumed was 2.07 c.c., equivalent to 0.68 per cent ammonium ($NH_4^+$).

*Acetic Acid.*—(a) Took 5 c.c. of original, made acid with phosphoric acid and distilled over volatile acid with steam, and titrated distillate. 50.53 c.c. of tenth normal sodium hydroxide was consumed, equivalent to 5.45 per cent acetic acid. (b) Five c.c. of original required 50.84 c.c. of tenth normal sodium hydroxide, equivalent to 5.50 per cent.

## ASTHMA-TABS

### A "Famous New Discovery" of Old, Long-Used and Dangerous Drugs

*(Extracted, with additions, from The Journal A. M. A., Sept. 27, 1924, p. 1018)*

The "Asthma-Tabs Laboratories" of Kansas City, Mo., conducts a piece of mail-order quackery in the sale of an alleged cure for asthma known as "Asthma-Tabs."

The point of contact between quack and victim is, as usual, the venal or careless newspaper or magazine which sells its advertising space to herald such lies as these:

> "Kills Hay Fever and Asthma Germs in Three Days."
>
> "Famous New Discovery, Asthma-Tabs, Succeeds After Everything Else Had Failed."
>
> "If you are short of breath, sneeze, wheeze, can't sleep at night—this wonderful new discovery will remove these troubles in a few days."

### THE TRIAL TREATMENT

In keeping with the traditions of the dispenser of nostrums through the mails, there is the orthodox "free trial treatment." Thus: "To prove that Asthma-Tabs will absolutely rid you of Asthma and Hay Fever . . . I will send you a regular $1 treatment of my famous home remedy absolutely free and postpaid." The rest of the advertising paraphernalia also runs true to form. Those who answer the advertisement and apply for the "trial treatment" receive the first of a series of "follow-up" letters, all signed "R. N. Townley," together with some other pieces of advertising and a small package of "Asthma-Tabs" containing 15 tablets.

One of the accompanying pieces of advertising is a booklet entitled: "How Science Has Conquered Asthma and Hay Fever," which purports to give the history of the epoch-making "discovery" of Asthma-Tabs. According to the booklet the author suffered from asthma and hay fever for twelve years. He tried "dozens of remedies and several physicians" without avail. Finally he went to a physician who "had made a special study of Asthma and Hay Fever" and the doctor took him into his confidence and told him "he had been working for years on an entirely new constitutional remedy for Asthma and Hay Fever" but had not yet perfected it as he "lacked adequate laboratory facilities." After two more years of "heart-breaking discouragements" and disappointments the goal was reached! The remedy is said to have been first tried on the author of the booklet: "the result was almost instantaneous"; within a month "every trace of asthma had vanished never to return!"

Because of the number of inquiries received about the nostrum and the report that toxic effects had followed its use, two original bottles of "Asthma Tabs" (Asthma Tab Laboratories, Kansas City, Mo.) were submitted to the Laboratory for examination. The weight of the tablets approximated one-half gram each. Qualitative tests indicated the presence of potassium, sulphate, iodide, arsenic (in trivalent form) and a trace of iron. No other substances were found.

The following quantitative determinations were made:

| | | |
|---|---|---|
| Moisture (loss on drying at 100 C.) | 0.0 | per cent. |
| Potassium ($K^+$) | 29.69 | per cent. |
| Iodide ($I^-$) | 53.42 | per cent. |
| Sulphate ($SO_4^{--}$) | 16.90 | per cent. |
| Arsenic (as $As_2O_3$) | 0.103 | per cent. |
| | 100.113 | per cent. |

From the foregoing, "Asthma Tabs" may be considered to consist essentially of potassium iodide 70 per cent, potassium sulphate 29.9 per cent and arsenic trioxide 0.1 per cent. From this is may be said that each "Asthma-Tab" contains the equivalent of:

| | | |
|---|---|---|
| Potassium iodide | 0.35 | Gm. (about 5½ grains) |
| Potassium sulphate | 0.15 | Gm. (about 2⅓ grains) |
| Arsenic trioxide (arseni trioxidum, U. S. P.) | 0.0005 | Gm. (about $\frac{1}{120}$ grain ) |

The adult dose recommended on the label is three tablets a day. This is equivalent to 1.05 Gm. (16.2 grains) of potassium iodide, 0.45 Gm. (6.9 grains) of potassium sulphate and 0.0015 Gm. ($\frac{1}{40}$ grain) arsenic trioxide (*arseni trioxidum* U. S. P.) daily.

Commenting on the analysis THE JOURNAL stated in conclusion:

> "And this is the 'Famous New Discovery' that 'Kills Asthma and Hay Fever Germs in Three days,' that 'contains no harmful drugs'—arsenic trioxide and potassium iodide, two drugs that have been used for generations in the treatment of asthma and two drugs that may easily be both harmful and dangerous when used without care or in ignorance of their presence. Is there any line of human activity in which dishonesty, chicanery and an utter disregard for the homely virtues of truthfulness and fair-dealing and even for human life itself is so rampant as it is in the 'patent medicine' business? If there is, we do not know of it."

### Details of Analysis

*Solution.*—3.4373 Gm. of the powdered tablets dissolved completely in 300 cc. of water. This was diluted to exactly 500 cc. in a volumetric flask.

*Potassium.*—An aliquot from the prepared solution was treated with 3 cc. of sulphuric acid and evaporated to dryness in a weighed platinum dish. The transformation of the bisulphate into the sulphate was effected with ammonium carbonate according to the ordinary procedure. (a) 25 cc. yielded 0.1137 Gm. of potassium sulphate, equivalent to 29.71 per cent potassium. (b) 25 cc. yielded 0.1136 Gm. of potassium sulphate, equivalent to 29.67 per cent potassium ($K^+$).

*Iodide.*—An aliquot of the prepared solution was treated with 15 cc. of diluted nitric acid and sufficient silver nitrate solution to precipitate all the iodide. The precipitate was allowed to settle in the dark and then transferred to a weighed Gooch crucible. The crucible and contents was dried at 100 C. and weighed. (a) 10 cc. yielded 0.0680 Gm. of silver iodide, equivalent to 53.47 per cent iodide (I ). (b) 10 cc. yielded 0.0676 Gm. of silver iodide, equivalent to 53.37 per cent iodide.

*Sulphate.*—An aliquot of the prepared solutions was diluted to 250 cc. and then treated with 1 cc. of hydrochloric acid and sufficient barium chloride solution to precipitate the sulphates. After digesting for five hours on the steam bath, the solution was filtered through a weighed Gooch crucible. The crucible and contents was dried at 120 C. for five hours, cooled in a desiccator and then weighed. (a) 25 cc. yielded 0.07093 Gm. barium sulphate, equivalent to 16.97 per cent sulphate ($SO^{--}$). (b) 25 cc. yielded 0.0704 Gm. barium sulphate, equivalent to 16.84 per cent sulphate ($SO^{=}$).

*Arsenic.*—About two grams accurately weighed was dissolved in about 40 cc. of diluted sulphuric acid. The solution was poured in the generator of a "Marsh Test" apparatus which had been operated about half an hour. During this half hour a blank test for arsenic was made and found negative. The arsenic was collected in a weighed fused silica arsenic tube. The tube was heated to redness during the run which lasted two hours. After this period the flame was withdrawn and a white porcelain crucible lid held in the hydrogen flame at the end of the arsenic tube. As no spot appeared, the tube was allowed to cool, then disconnected and weighed. (a) 1.5333 Gm. yielded 0.00131 Gm. arsenic (As); this is equivalent to 0.112 per cent arsenious oxide ($As_2O_3$). (b) 2.0774 Gm. yielded 0.0015 Gm. arsenic (As); this is equivalent to 0.095 per cent arsenious oxide ($As_2O_3$).

*Moisture.*—A sample kept at 100 C. for two hours showed no appreciable loss in weight.

## B. PAUL'S HENNA AND LIQUID HAIR DYES

### Two More Hair Dyes

*(Extracted, with additions, from The Journal A. M. A., Nov. 1, 1924, p. 1449)*.

Two hair dyes are put out by one Paul Balme, who does business in New York City under the name "B. Paul." One of these dyes is known today as "B. Paul's Henna" and is a powdered mixture. The other, put out by the same man, is called "B. Paul's Liquid Mixture." The nostrum that is now known as "B. Paul's Henna" was sold by Balme for some years as "Henna d'Oreal," an alleged "New French Discovery" described as "La Plante Merveilleuse." In April, 1922, Paul Balme was ordered by the Federal Trade Commission to cease using the word "Oreal" and also the phrase "La Plante Merveilleuse," as both of these terms had been in use for some years before Balme put his hair dye on the market by another concern also in the hair dye business.

### "B. PAUL'S HENNA"

This comes in a tin can on which appears the following claims:

> "Nature's Hair Regenerator"
>
> "The Wonder Herb, Nature's Hair Restorer"
>
> "B. Paul's Henna is a powdered preparation composed of pulverized henna and herbs which will color gray hair to any one of our fourteen different shades"

The can is about seven-eighths filled with a yellowish powder. There is also a small envelope of oil paper containing a white powder and labeled "B. Paul's Developer: to set the shade." The directions with "B. Paul's Henna" are that the hair must first be washed and left damp. Then the powder is to be made into a thick paste with boiling water. This pasty mess is then applied to the hair and left on for a time varying from thirty minutes to two hours, according to the depth of shade required. After the application, the hair is to be rinsed until all the paste is out and then rerinsed in a solution made by dissolving the white powder labeled "B. Paul's Developer." The hair then is to be shampooed again.

An original can of "B. Paul's Henna" prepared by B. Paul New York, was submitted to the Laboratory for examination. The can contained a paper bag containing 117 Gm. of a yellow powder; also a small sealed, oiled-paper package containing four grams of white crystalline material.

*Yellow Powder.*—Qualitative tests indicated the presence of iron, copper, sulphate, pyrogallol and vegetable matter. Quantitative determinations yielded the following results:

| | |
|---|---|
| Iron ($Fe^{+++}$) | 6.8 per cent. |
| Copper ($Cu^{++}$) | 3.32 per cent. |
| Pyrogallol | 3.86 per cent. |
| Ash | 19.88 per cent. |

*White Powder.*—This material appeared to be sodium perborate ($NaBO_3.4H_2O$), with a trace of sodium carbonate. Quantitative determinations showed boron 7.27 per cent and available oxygen 9.59 per cent. These are in close agreement with the theoretical amounts for sodium perborate, *i. e.*, boron 7.09 per cent and available oxygen 10.39 per cent.

From the foregoing it may be assumed that B. Paul's Henna is (1) a powder consisting essentially of dried plant leaves, pyrogallol and iron and copper compounds, and (2) a second package containing sodium perborate, a substance, which, when treated with water, yields hydrogen peroxide.

As THE JOURNAL stated:

"The whole trend of the advertising is to lead the public to believe that 'B. Paul's Henna' is purely herbal. As a matter of fact, when examined in the Association's chemical laboratory, the stuff was found to contain, in addition to the powdered herbs, iron, copper, and pyrogallol, while the 'developer' sold as an accessory was found to be sodium perborate. As for its alleged harmlessness, neither pyrogallol nor copper salts are innocuous. Germany is said to prohibit the use of copper salts in hair dyes."

### B. PAUL'S LIQUID MIXTURE

As has been mentioned, B. Paul, in addition to putting out a powdered hair dye, also puts one out in liquid form. The liquid preparation is advertised in the circular of directions for the use of "B. Paul's Henna." The liquid product is said to be especially adapted "for touching up the roots near the scalp" and is recommended to those who do not care to use a paste form of hair dye but prefer a liquid. The circular also has this to say about "B. Paul's Liquid Mixture":

> "This coloring is superior to any liquid dye on the market and is absolutely harmless, being a vegetable compound."

A circular that comes with the trade package gives directions for its use. These are to the effect that the liquid contained in the bottle marked "A" (it is a two-liquid preparation) is to be applied to the hair thoroughly and allowed to dry. Then the liquid contained in the bottle marked "B" is similarly applied.

An original sample of "B. Paul's Liquid Mixture for Coloring Gray Hair" was submitted to the Laboratory for analysis. The mixture was contained in two brown bottles labeled "A" and "B," respectively, and each containing 95 cc. (approximately 3 fluid ounces).

*Bottle "A."*—This contained a dark blue liquid of ammoniacal odor. Qualitative tests indicated the presence of copper, ammonia, sulphate, and a trace of iron. The specific gravity of the liquid in Bottle "A" was 1.004. The amount of solids present found was 0.90 per cent and the amount of ash was 0.19 per cent. Quantitative determinations were as follows:

| | |
|---|---|
| ($Cu^{++}$) | .23 per cent |
| ($SO_4^{--}$) | .41 per cent. |
| ($NH_3$) | .43 per cent. |
| Water (by difference) | 98.93 per cent. |
| | 100.00 per cent. |

The product is essentially a solution of the well known cupric ammonium sulphate made by treating a solution of cupric sulphate with ammonia water. A solution similar to Solution "A" could be made by dissolving 1 Gm. of commercial copper sulphate ("blue vitriol") in 90 cc. of water and adding 4 cc. of ammonia water, U. S. P.

*Bottle "B."*—This appeared to be a solution of pyrogallol which had undergone some decomposition. The specific gravity of the solution was 1.029. Quantitative estimations were as follows:

| | |
|---|---|
| Pyrogallol | 9.67 per cent. |
| Decomposition products | 0.95 per cent. |
| Loss in weight (at 100 C.) | 88.53 per cent. |
| Difference | 0.85 per cent. |
| | 100.00 per cent. |

A solution similar to Solution "B" could be made by dissolving 11.2 Gm. pyrogallol in sufficient water to make 95 cc.

THE JOURNAL stated:

"Again the findings of the chemists disagree with the claims made by the exploiter. B. Paul's Liquid Mixture is neither a vegetable compound nor 'absolutely harmless'."

## Details of Analysis

### B. Paul's Liquid Mixture

### Solution "A"

*Specific Gravity.*—The specific gravity at 15°C. was 1.004.

*Sulphate.*—(a) Five cc. of the original was diluted to 250 cc. Sufficient diluted hydrochloric acid was added to dissolve the precipitated copper hydroxide and then 1 cc. of concentrated hydrochloric acid was added. Barium chloride solution was added to precipitate all of the sulphate. After allowing the solution to set over night, the precipitate was filtered onto a weighed Gooch crucible and dried at 100 C. for five hours, cooled in a desiccator, and weighed. The weight of barium sulphate was 0.0495 Gm., equivalent to 0.406 per cent sulphate ($SO_4=$). (b) Five cc. yielded 0.0511 Gm. barium sulphate, equivalent to 0.418 per cent sulphate ($SO_4=$).

*Copper.*—(a) Ten cc. of the original was transferred to a weighed platinum dish, sufficient diluted nitric acid added just to dissolve the copper hydroxide. 2.5 cc. of concentrated nitric acid was then added and the solution diluted to approximately 50 cc. The solution was electrolyzed, the dish serving as the cathode and a platinum wire spiral as the anode, using 2.2 volts for three hours. The liquid was then siphoned from the dish, distilled water being added at the same time until only a negligible amount of current was passing through the solution. After washing with (1) distilled water; (2) alcohol, and (3) ether, the dish was dried and then weighed. The weight of copper was 0.0240 Gm., equivalent to 0.23 per cent. (b) 10 cc. yielded 0.02388 Gm. of copper, equivalent to 0.23 per cent.

*Ammonia.*—10 cc. of the original was transferred to a distillation flask, 40 cc. of water and 10 cc. of sodium hydroxide solution added. The ammonia was aspirated into a known quantity of standard acid, the whole aspiration consuming approximately one hour. The flask was gently heated at first while at the end boiling was allowed. The acid was titrated with normal sodium hydroxide using alizerin red as an indicator. The amount of tenth normal acid consumed was 2.52 cc., equivalent to 0.42 per cent ammonia ($NH_3$). 10 cc. of the original required 2.59 cc. of normal hydrochloric acid, equivalent to 0.44 per cent ammonia ($NH_3$).

*Total solids.*—The residue obtained by evaporating 5 cc. on the water bath was 0.0452 Gm., equivalent to 0.90 per cent.

*Ash.*—The ash from 5 cc. was 0.0096 Gm., equivalent to 0.19 per cent.

### Solution "B"

*Solids.*—10 cc. of the solution was evaporated to dryness on the steam bath. The dish was cooled in a desiccator and then weighed. 1.180 Gm. is equivalent to 11.47 per cent.

*Pyrogallol.*—The solid material obtained above was extracted three times with ether. The ether was evaporated leaving a white crystalline solid weighing 0.9956 Gm., equivalent to 9.67 per cent. This was shown to be pyrogallol.

*Decomposition Products.*—The material insoluble in ether was an amorphous substance that was not tannin. It was dried on the water bath and in a desiccator and weighed. 0.0987 Gm. is equivalent to 0.95 per cent.

## B. PAUL'S HENNA

### Henna

1.6574 Gm. of the powder was ashed in a quartz dish. The residue was heated with aqua regia and the chlorine expelled by boiling to a small bulk twice after having added nitric acid. The nitric acid solution was then diluted, filtered and diluted to exactly 250 cc. in a calibrated volumetric flask.

*Copper.*—50 cc. of the solution prepared above was neutralized with ammonium hydroxide. Diluted nitric acid was added until the precipitate just dissolved and then 1 cc. of concentrated nitric acid was added. The solution was evaporated to about 30 cc., transferred to a weighed platinum dish and electrolyzed for four hours, using 2.2 volts. Water was added and the solution was siphoned off until a very small current was flowing. The current was then broken, the dish washed with water followed by alcohol and then dried by holding it high over a flame. After cooling in a dessicator, it was weighed. (a) 50 cc. of the prepared solution yielded 0.0112 Gm. of copper, equivalent to 3.37 per cent copper ($Cu^{++}$). (b) 50 cc. of the prepared solution yielded 0.0109 Gm. of copper, equivalent to 3.28 per cent copper ($Cu^{++}$).

*Iron.*—Five cc. of ammonium chloride solution was added to 50 cc. of the prepared solution and then made strongly ammoniacal. The solution was digested on the water bath for forty-five minutes. The precipitate was thrown on a weighed Gooch crucible and washed until the water showed the absence of chlorides. The crucible was dried in an oven at 120 C. over night, and then heated to constant weight over a Tirrill burner. The ferric oxide residue weighed 0.0332, equivalent to 7.0 per cent iron ($Fe^{+++}$). (b) 50 cc. of the solution yielded .0319 Gm. ferric oxide, equivalent to 6.7 per cent iron ($Fe^{+++}$).

*Ash.*—The ash was determined by heating a weighed quantity of the material in a quartz dish over a blast lamp. 1.6574 Gm. of the powder yielded 0.3295 Gm. ash, equivalent to 19.88 per cent ash.

### Developer

*Boron.*—The determinations were made according to the method described in the Annual Reports of the Chemical Laboratory of the American Medical Association **10**:7.

1.7541 Gm. of the original was dissolved in 100 cc. of water and the solution diluted to exactly 250 cc. (a) 50 cc. of this solution was made just acid to methyl red using normal hydrochloric acid. The solution was heated and boiled for one minute after which it was cooled to about 70 C. and exactly neutralized with tenth normal sodium hydroxide. 40 cc. of neutral glycerin was then added and the solution was titrated, using phenolphthalein as indicator. 23.54 cc. was consumed, equivalent to 7.31 per cent boron. (b) Another 50 cc. aliquot took 23.28 cc. tenth normal sodium hydroxide. This is equivalent to 7.23 per cent boron.

*Oxygen.*—Weighed samples of the material (about 0.12 Gm.) were dissolved in 40 cc. of cold water to which 10 cc. of one to one sulphuric acid was added. The solution was titrated immediately with N/10 $KMnO_4$. (a) 0.0844 Gm. of developer required 10.18 cc. of N/10 $KMnO_4$, equivalent to 9.64 per cent active oxygen. (b) 0.1233 Gm. of developer required 14.73 cc. of N/10 $KMnO_4$, equivalent to 9.55 per cent active oxygen.

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## CLEERO

### Quackery in Shampoos

*(Abstracted, with additions, from The Journal A. M. A., Nov. 15, 1924, p. 1607)*

"Cleero," which is labeled "the vanishing shampoo," is put out by the Van Ess Laboratories of Chicago.

The thesis advanced by the Van Ess Laboratories for the use of Cleero is that the use of soap on the hair is dangerous and that "the free alkali present in most soaps" makes them still worse. Danger, one is told, also lies in the rinsing, for water is said "to devitalize the hair." More than this, the Van Ess concern says that most city water "contains harsh chemicals injected to combat drinking germs" and that these chemicals are very hard on the hair. It would be interesting to learn what the Van Ess Laboratories think these same chemicals, which are said to be injurious to such a hornlike substance as hair, must do to the delicate mucous membrane of the alimentary canal.

The advertising that goes with the trade package of Cleero leads the purchaser to believe, without actually making the definite statement, that Cleero is not a soap. The circular definitely states that "Cleero contains no free alkali."

Cleero is recommended for oily hair because it is claimed that it "almost instantly dissolves and removes this excessive natural oil." It is recommended for dry hair because "dry hair absorbs a sufficient portion of the pure vegetable oils in Cleero" to make it oily. It is recommended for white hair because it "intensifies its natural beauty," and it is recommended for dyed hair.

Because of inquiries received, specimens of Cleero were purchased, the product was analyzed and the following report published:

One original bottle of Cleero (Van Ess Laboratories, Chicago) was submitted to the Laboratory for examination. The bottle contained about four fluid ounces of a pale yellow, perfumed liquid having an odor of ammonia. The liquid had a strongly alkaline reaction to litmus.

Qualitative tests indicated the presence of a soap having the characteristics of a cocoanut oil soap, free ammonia, an ammonium salt, carbonate, potassium, glycerin and a trace of sodium and of chloride. The carbonate is evidently present as ammonium carbonate. The potassium is a constituent of the cocoanut oil soap. The perfume probably consists largely of oil of lavender, or an imitation having a lavender-like odor. The amount of glycerin present is approximately ten per cent.

Heavy metals (such as lead and mercury) and such substances as sodium borate (borax), sucrose (cane sugar), magnesium sulphate, egg albumen, quillaja extractives, calcium salts, quinine and other alkaloids were not found.

Quantitative analysis of Cleero gave the following:

| | |
|---|---|
| Specific gravity (at 25C./25C.) | 1.040 |
| Solids on drying | 27.86 gm. per 100 c.c. |
| Ammonia ($NH_3$) | 1.04 gm. per 100 c.c. |
| Potassium ($K^+$) | 2.41 gm. per 100 c.c. |
| Fatty acids (from soap) | 13.08 gm. per 100 c.c. |

"The results of the examination indicate that Cleero is essentially a perfumed, watery solution of soap with free alkali and glycerin having approximately the following composition:

| | |
|---|---|
| Cocoanut oil soap | ½ ounce |
| Ammonium carbonate ("hartshorn") | ⅒ ounce |
| Glycerin | ⅓ ounce |
| Water | 3⅓ ounces |

Concerning Cleero and its composition, The Journal commented as follows:

"From the chemists' investigation, it is obvious that Cleero, which is recommended to take the place of soap, is a soap and that the free alkali which is said to be so harmful for the hair is present in Cleero. If a mixture of soap, hartshorn, glycerin and water is the best in the way of new discoveries that 'the most exclusive beauty parlors of the old Continent' can produce, the old Continent must be slipping. However, so long as the American public can be persuaded to part with perfectly good money for a very ordinary mixture put out under extraordinary quackish claims, the Van Ess Laboratories will assume that truth in advertising is but a phrase that has merely academic interest."

### Details of Analysis

*Specific Gravity at 25 C./25 C.*—The specific gravity of the solution was taken with a pycnometer. A volume of 24.9732 c.c. weighed 25.9929 Gm., corresponding to a specific gravity of 1.0408. The liquid in the pycnometer was mixed with water and the solution made up to 500 c.c. Aliquot portions of this were used for various determinations.

*Ammonia.*—An excess of potassium hydroxide was added to 50 c.c. of the diluted solution, equivalent to 2.4973 c.c. of original material, and the ammonia distilled into a measured excess of normal hydrochloric acid, diluted with five volumes of water. The excess of acid was titrated with tenth-normal potassium hydroxide in the usual way. The results were calculated to free ammonia, and to ammonium carbonate. The ammonia from 50 c.c. of the diluted solution required 1.61 c.c. of normal hydrochloric acid, equivalent to 1.06 Gm. of ammonia ($NH_3$) per 100 c.c. A duplicate required 1.55 c.c. of normal acid, equivalent to 1.01 Gm. of ammonia per 100 c.c. Average 1.035 Gm. of ammonia per 100 c.c. This is equivalent to 3.18 Gm. of ammonium carbonate of the approximate formula given by the U. S. P. IX.

*Fatty Acids from Soap.*—Fatty acids were determined by acidifying the diluted solution with sulphuric acid, shaking with ether, evaporating the solvent and weighing. From 100 c.c. of the diluted solution, equivalent to 4.9946 c.c. of original material, a weight of 0.6727 Gm. of fatty acids was obtained, equivalent to 13.07 Gm. per 100 c.c. Fifty c.c. of original material gave 6.5454 Gm. of fatty acids, equivalent to 13.0908 Gm. per 100 cc. Average, 13.08 Gm. of fatty acids per 100 cc.

*Potassium.*—The acidified solution from the fatty acid determination was evaporated to dryness in the presence of an excess of sulphuric acid, the residue heated to redness and afterward heated with a fragment of ammonium carbonate to constant weight. The sulphuric acid in the residue was afterward determined and calculations made to determine whether or not sodium was present. The sulphate from 100 c.c. of the diluted solution weighed 0.2771 Gm., equivalent to 0.1243 Gm. of potassium. This is equivalent to 2.409 Gm. of potassium per 100 c.c. of original material. A determination of the sulphate in this residue by weighing as barium sulphate in the usual way indicated that the metal in the soap is potassium with little or no sodium.

*Soap.*—The sum of the free fatty acids (13.08 Gm. per 100 c.c.) and the potassium (2.4 per cent.) is 15.49 Gm. per 100 c.c. This represents the soap originally present in the mixture. The iodine number and the saponification number of the free fatty acids were determined using the methods described in the U. S. P. IX for the determination of those constants. A weight of 0.2622 Gm. of material consumed iodine equivalent to 2.19 c.c. of tenth normal iodine. This is equivalent to an iodine absorption number of 10.6. According to Benedikt and Ulzer (p. 874, 1908) the iodine number of the fatty acids from cocoanut oil varies from 8.3 to 9.3. A weight of 0.6727 Gm. of the fatty acids required 30.95 c.c. of tenth normal potassium hydroxide, equivalent to a combining number of 259.86. According to Benedikt and Ulzer (*Ibid.*) the combining number of the mixed fatty acids from cocoanut oil varies from 258 to 273.3. From these findings, as well as from the physical appearance of the separated fatty acids, it was concluded that the fatty acid constituent of the soap in Cleero had been derived from cocoanut oil.

*Carbonate.*—Some of the original material was acidified with sulphuric acid and the resultant mixture boiled. The evolved gas was passed through barium hydroxide solution; a white precipitate was formed. The amount of carbon dioxide was not determined.

*Glycerin.*—This was determined approximately by removing the fatty acids by means of sulphuric acid and ether as described under "fatty acids" above, evaporating the acid solution to dryness after adding ammonia water, macerating the residue with alcohol, adding ether to the filtrate from the maceration, filtering, evaporating on a simmering steam bath and weighing. The residue was burned and the ash subtracted from the first weight. This method is an approximation only as some ammonium salts were carried through and weighed as glycerin. The weight of crude glycerin from 15 c.c. of original material was 1.1776 Gm. and the ash from this residue amounted to 0.0044 Gm. This difference is equivalent to 11.8 Gm. of glycerin per 100 c.c. of original material. The glycerin from 50 c.c. of original material weighed 2.8768 Gm. and the ash 0.3633. The net weight of the glycerin was 2.5135 Gm., or 10.05 Gm. per 100 c.c. Both of these glycerin residues contained ammonium salts, but the quantity was not determined. From the results obtained it is concluded that the amount of glycerin in the preparation is approximately 10 per cent.

## PAINODYNES AND NEURODYNE

A query and the following reply were published in The Journal A. M. A., Nov. 22, 1924, p. 1705, after preliminary tests in the laboratory:

*To the Editor:*—I have received several advertisements from the William A. Webster Company concerning their Painodynes, in which they printed their purported formula of the preparation. I am not particularly interested in it, as I generally find everything I need in our regular materia medica; but, out of curiosity, I wrote and asked them what their "Neurodyne" is, as it seems to be the important ingredient in the mixture. They sent me the enclosed letter, which you will note is full of meaty information, but which must go over the heads of most of the profession, as it does over mine. If you can translate this long chemical name into words of one syllable, it may save a lot of headaches in those who might go to the trouble of trying to look it up in a textbook on chemistry, and will probably save me from the fate suffered by the famous cat, to whom curiosity proved lethal. J. B. H., M.D., Nevada.

Answer.—According to the label on the bottle, Painodynes (sold by the William A. Webster Company, Memphis, Tenn.) consists of "An organic compound containing Neurodyne 5 grains, Theine Citrated ½ grain combined with triple bromides ½ grain." The letter of "information" sent our correspondent by the Webster concern regarding Neurodyne is as follows:

> For your information will advise that Neurodyne (Ortho Hydroxybenzoic Acetic Acid Ester) which is an analgesic and anodyne of the highest order. And it might be incidentally stated that this compound as used in the manufacture of Painodynes is of the highest degree of purity—being entirely free from injurious by-products and other impurities. Thus, the utmost beneficial effects of the drugs are obtained without untoward results.

Ortho Hydroxybenzoic Acetic Acid Ester is a ridiculously long drawn out name for acetylsalicylic acid (aspirin). Tests made in the Laboratory indicated the presence of this substance in Painodynes. The firm's statement that the compound "is of the highest degree of purity—being entirely free from injurious by-products and other impurities" could not be confirmed, as the amount of free salicylic acid in the specimen examined was much greater than that permitted for the various brands of acetylsalicylic acid described in New and Nonofficial Remedies. Furthermore, the Laboratory, using an extremely sensitive test, was unable to find any "citrate" present, although "Theine citrated" is declared.[1] (Theine is a little-used name for caffeine.) These discrepancies, however, are not surprising, as the firm has pleaded guilty in the District Court of the United States a number of times to the charge of adulteration and misbranding—and one of the products was Aspirin Tablets! On the face of it, the product itself belongs to the class of irrational shotgun mixtures, marketed with unwarranted claims.

An article discussing the William A. Webster Company (and the Direct Pharmaceutical Company of St. Louis, apparently a sales agency) appeared in THE JOURNAL, Oct. 18, 1919, p. 1231.

## "SAN-GRI-NA"

### Another Fake Obesity Cure

*(Abstracted, with additions, from The Journal A. M. A., Nov. 22, 1924, p. 1703)*

> "San-Gri-Na is the formula of a French physician. It has been used in Europe by millionaires, actresses and hundreds of fat men and women because it is simple, easy, pleasant and harmless."

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[1] The bottle contained 100 tablets, light green in color, weighing approximately 0.4 gm. each. On opening the bottle, the odor of acetic acid was discernible. In testing for free salicylic acid, a calculated amount of caffeine citrate was added to the standard tube to simulate "claimed" composition of "Painodynes." On addition of small amount of ferric chloride solution, there was no color in the standard, although there was color in the "Painodyne" solution; this aroused suspicion as to presence of citrate in "Painodynes." A delicate test was therefore worked out (see p. 50), which demonstrated the absence of citrate.

Thus runs part of the advertising claptrap of San-Gri-Na, one of the recent entrants to the "obesity cure" field. San-Gri-Na is put out by the somewhat imposingly named "Scientific Research Laboratories" of 350 West Thirty-First Street, New York City. Apparently the Scientific Research Laboratories is merely a name for the mail-order business which is said to be conducted in a loft at the address given.

San-Gri-Na is exploited in the manner common to quackery of this type. It is said to be the "amazing discovery" of a "Dr. Narbonne," who is described as a famous French scientist. Part of the advertising paraphernalia consists in what purports to be a letter from Madame Elaine of Paris. This details to the gullible obese just how Madame reduced herself 50 pounds in two months' time by the San-Gri-Na method.

In addition to being sold on the mail-order plan, San-Gri-Na is also on sale in the drug stores, and expensive newspaper advertisements lure the "stylish stouts" to the local drug counter. San-Gri-Na comes in tablets, and the concern that puts it out seems to find no difficulty in relieving the public of $1.50 for fifty of these tablets. With each box comes a small leaflet giving the alleged theory on which the tablets act, together with instructions for taking them. According to this leaflet, "Dr. Narbonne," the "famous French scientist," discovered in the course of his researches that in all fat people "there exists a certain condition in their systems which transforms their food into flabby fat instead of enriching their blood by making healthy, red corpuscles." A man from Mars might suppose that it would be impossible in this year of grace, when at least the rudiments of physiology are taught in school, to find people who would swallow such egregious nonsense as that just quoted. But a generation which accepts chiropractic, the Electronic Reactions of Abrams, "Christian Science," Naturopathy and similar nonsense may be excused for taking seriously the San-Gri-Na school of physiology.

The newspaper advertisements convey to the obese public the idea that it is unnecessary to exercise or diet, the only desideratum being the purchase of San-Gri-Na. When the stuff has been bought, however, the purchaser finds that in addition to taking San-Gri-Na she should take the juice of one lemon in a glass of warm water every morning, chew her food very thoroughly, eat only two or three light meals a day, sleep not more than six or seven hours, do a "reasonable amount of walking," take no liquid with meals, avoid starches, fats and candy! The instructions remind one of the lady who found great relief from constipation by reading two chapters of "Science and Health" daily—and taking a dose of salts.

Specimens of San-Gri-Na were purchased on the open market for analysis:

Four original packages of San-Gri-Na, manufactured by the Scientific Research Laboratory, New York, were submitted to the Chemical Laboratory for examination. Each package contained fifty yellowish-gray tablets having an average weight of 0.42 Gm. (6½ grains) each. No information concerning the composition of San-Gri-Na appeared on the label of the preparation or in the circulars accompanying the package, except the statement that it did not contain any habit forming drugs. An aqueous extract of the powdered tablets gave an acid reaction to litmus. Tests indicated the presence of free sulphur, phenolphthalein, calcium, potassium, small amounts of sodium, carbonate, tartrate, starch, traces of reducing sugar, and an acid-soluble substance, probably talc. A vegetable extractive, which had a faintly bitter taste, but no other distinctive properties, was present. Under the microscope the starch was identified as derived from arrowroot.

No alkaloids, emodin-bearing drugs, such as cascara, senna and rhubarb, heavy metals, ammonium salts, strontium salts, magnesium salts, sucrose (cane sugar), lactose (milk sugar), nitrates, chlorides, bromides, iodides, organically combined iodine, sulphates, phosphates or glycyrrhiza were found. Neither were there found any extracts from thyroid and bladderwrack, drugs sometimes used in obesity remedies. The ash had an alkaline reaction to litmus paper and contained sulphates, due to the oxidation of sulphur in the presence of alkalis.

Quantitative analysis of San-Gri-Na gave the following results:

| | |
|---|---|
| Moisture | 2.84 per cent. |
| Ash | 35.37 per cent. |
| Acid-insoluble ash (talc) | 3.61 per cent. |
| Phenolphthalein | 2.11 per cent. |
| Sulphur | 32.93 per cent. |
| Calcium ($Ca^{++}$) | 4.49 per cent. |
| Sodium ($Na^{+}$) | 0.63 per cent. |
| Potassium ($K^{+}$) | 4.62 per cent. |
| Tartrate ($C_4H_4O_6{=}$) | 16.26 per cent. |
| Starch | 10.80 per cent. |

The calcium was calculated to calcium carbonate and the tartrate to potassium bitartrate. A determination of the tartrate radical and calculation to potassium bitartrate gave slightly lower results than if all the potassium had been calculated to potassium bitartrate. It seems probable that this small excess of potassium and the sodium are derived from the plant extractive present. From the results of the analysis, the composition of San-Gri-Na may be calculated to be essentially as follows:

| | |
|---|---|
| Sulphur | 33 per cent. |
| Potassium bitartrate (cream of tartar) | 21 per cent. |
| Vegetable extractive and undetermined | 15 per cent. |
| Calcium carbonate (precipitated chalk) | 11 per cent. |
| Arrowroot starch | 11 per cent. |
| Talc | 4 per cent. |
| Moisture | 3 per cent. |
| Phenolphthalein | 2 per cent. |

Sulphur and cream of tartar constitute a well known, slightly aperient mixture in medicine. The two substances are mixed in various proportions but are not combined with phenolphthalein or precipitated chalk. The formula described in the National Formulary "Troches of sulphur and potassium bitartrate" contains five times as much sulphur as cream of tartar. In San-Gri-Na the sulphur is present in about the proportion of three to two. A daily dose of 6 tablets of San-Gri-Na contains about ¾ grain of phenolphthalein, 13 grains of sulphur and 8 grains of cream of tartar. The average single dose as given in the U. S. Pharmacopeia for each of these drugs is 2½ grains, 60 grains and 30 grains, respectively.

Concerning San-Gri-Na and the methods used in exploiting it THE JOURNAL commented as follows:

"In the light of the chemists' analysis, it seems that the amazing discovery of the famous French scientist is essentially sulphur and cream of tartar, with a small quantity of the laxative phenolphthalein. Various large pharmaceutical houses of the country carry in stock tablets of sulphur and cream of tartar, which are quoted at 35 cents a hundred.

"The public may ask, What is there about San-Gri-Na tablets that will reduce? The answer is, nothing; they won't reduce. There are always optimistic overweights, however, who will willingly part with good money for anything, however worthless, that may be recommended for weight reduction. This ever hopeful army of easy marks makes the obesity cure game a profitable one."

### Details of Analysis

*Phenolphthalein and Sulphur.*—A weighed portion of the material was extracted with chloroform-ether mixture (9 to 1 by volume) in a Soxhlet apparatus until extraction was complete. The solvent was evaporated on a water bath, the residue treated with anhydrous ether, the solvent evaporated and the residue dried for a short time at 100 C. It was found that drying at 100 C. caused a small and approximately constant loss owing, probably, to the slow oxidation of sulphur. From 1.5704 Gm. of material a weight of 0.5343 Gm. was obtained, equivalent to 34.39 per cent. of chloroform-ether soluble material. From 0.6936 Gm. of material from another lot of tablets, a chloroform-ether-soluble extract was obtained which weighed 0.2475 Gm., equivalent to 35.68 per cent. Average, 34.85 per cent chloroform-ether-soluble material. The residue from the chloroform-ether extraction was treated by repeated stirring with an excess of dilute sodium hydroxide solution (about 1 per cent.) and the solution decanted through a filter into a separator. After repeated extraction with the dilute alkali until the fresh solvent no longer became pink, the solution was acidified with hydrochloric acid and shaken repeatedly with ether until extraction was complete. The solvent was washed with water after each shaking, the wash water being added to the bulk of the aqueous solution previously extracted. The ether was evaporated at ordinary temperature by the aid of a fan. The residue was dried at 100 C. and weighed. The ether extract from 0.6936 Gm. of original material weighed 0.0139 Gm., or 2.00 per cent. The ether extract from 1.5704 Gm. of material weighed 0.0347 Gm., equivalent to 2.21 per cent. Average, 2.11 per cent. of phenolphthalein. Sulphur was estimated by difference between the total chloroform-ether extract and the phenolphthalein found, i.e., 35.68 per cent. −2.00 per cent. = 33.68 per cent. of sulphur; 34.39 per cent. −2.21 per cent. = 32.18 per cent. of sulphur. Average, 32.93 per cent. of sulphur.

*Phenolphthalein, Identification of.*—A fragment of the residue after separation from sulphur was treated with sulphuric acid; a red color appeared instantly.

Another portion of the residue was dissolved in a slight excess of sodium hydroxide; a deep red solution was produced; this color disappeared on heating.

An excess of sodium hydroxide solution was added to a portion of the red solution obtained as above described and the mixture warmed until it had acquired a pale yellowish tint. An excess of iodine solution was added, followed by an excess of hydrochloric acid. The brown precipitate which formed was collected on a filter, washed with 5 c.c. of water and the residue dissolved in 5 c.c. of diluted sodium hydroxide solution. A purplish blue solution resulted.

That the residue supposed to be phenolphthalein was not phenolphthalein diacetate or salicylate was proved by the following procedure: A portion of the residue was boiled with an excess of alcoholic potassium hydroxide, the alcohol evaporated and the residue taken up in water. On acidifying a portion of the solution with sulphuric acid and boiling, no odor of acetic acid was obtained. Another portion of the solution after treatment was acidified and a drop of ferric chloride solution added. No violet color resulted.

*Sulphur, Identification of.*—The chloroform-ether extract of the material after treatment with sodium hydroxide solution to remove phenolphthalein was dissolved in warm chloroform. On standing in a place protected from dust where the chloroform could evaporate slowly, yellow, octahedral crystals were obtained which under the microscope appeared to be exactly like those obtained from a known specimen of sulphur after similar treatment. A portion of the crystalline residue obtained as above described burned with a pale blue flame and emitted an odor like sulphur dioxide. A small quantity of the material was digested in the cold with a very concentrated solution of potassium hydroxide for several hours. A drop of this material was diluted with 2 c.c. of water and a few drops of sodium nitro-prusside solution added. A deep bluish-violet color appeared at once. These tests demonstrate the presence of elemental sulphur in the material examined.

*Potassium Bitartrate.*—Some of the material was shaken with cold water and the mixture filtered at once. The filtrate had an acid reaction to litmus. Some of the material which had previously been treated with chloroform-ether mixture in the extraction of sulphur and phenolphthalein was macerated with 1 per cent. sodium hydroxide for one hour, the solution decanted through a filter, the filtrate acidulated with acetic acid and the solution evaporated to a small volume. A few drops of glacial acetic acid and sufficient alcohol to make the mixture contain about 50 per cent. of alcohol were added. On standing over night, rhombic crystals were obtained which under the microscope appeared to be identical with the crystals obtained by recrystallizing potassium bitartrate from warm water containing a little acetic acid and alcohol. Some of the crystals were collected by decanting the supernatant liquid and washing the residue with cold water. The crystals were dissolved in hot water, the solution cooled and the test for tartaric acid applied as described in The Reports of the Chemical Laboratory A. M. A., Vol. 14, 1921, p. 47. The solution gave a violet color. These tests coupled with the fact that the ash of San-Gri-Na contained potassium, were taken to indicate the presence of potassium bitartrate in San-Gri-Na.

The method for the determination of potassium bitartrate which was used was as follows:

> A weighed portion of the material (1 to 2 Gm.) was extracted with chloroform-ether mixture in a Soxhlet apparatus as described above and the residue extracted with 1 per cent. sodium hydroxide until the extract no longer showed a pink color. The alkaline extract was acidified with acetic acid and the solution evaporated to 25 c.c. About 1 c.c. of glacial acetic acid was added, followed by 25 c.c. of alcohol. The mixture was allowed to stand 48 hours, the crystalline precipitate collected on a filter and washed twice with 50 per cent. alcohol. The filter and contents were dissolved in hot water and the solution titrated with tenth-normal potassium hydroxide, using phenolphthalein as indicator.

The potassium bitartrate obtained from 1.5704 Gm. of material required 17.05 c.c. of tenth-normal potassium hydroxide, equivalent to 20.43 per cent. of potassium bitartrate in the original material. A duplicate of 1.0575 Gm. of material gave a precipitate which required 11.59 c.c. of tenth-normal potassium hydroxide, equivalent to 20.61 per cent. of potassium bitartrate in the original material. Average, 20.57 per cent of potassium bitartrate.

*Starch.*—A weighed quantity of the material was extracted with chloroform-ether mixture to remove sulphur and phenolphthalein, followed by 1 per cent. sodium hydroxide to remove potassium bitartrate, and then by water. The residue was then dried and heated to constant weight at a temperature below redness. It was believed that calcium carbonate was not affected by this treatment and that only the starch remaining was burned. A separate portion of the material treated as above up to the point of drying was examined under the microscope. The starch particles appeared to be identical with a known specimen of arrow root starch. From 1.0931 Gm. of material a loss of 0.1179 Gm. was obtained, equivalent to 10.79 per cent. of starch. From a duplicate of 1.5704 Gm. of material a loss of 0.1744 Gm. was obtained, equivalent to 10.80 per cent of starch. Average, 10.80 per cent of starch.

*Ash.*—A weighed portion of the material was heated to low redness, the residue cooled, macerated with water, the solutions decanted through a quantitative filter, the filter dried at 100 C. and finally at 120 C. and the residue heated to burn the remaining carbon. The filtrate was then added, the solution evaporated and the residue heated to constant weight.

The ash from 0.7190 Gm. of material weighed 0.2514 Gm., equivalent to 34.96 per cent. In another determination the ash from 2.1276 Gm. of material weighed 0.7615 Gm., equivalent to 35.79 per cent. Average, 35.37 per cent ash. As would be expected the ash contained sulphates in relatively large amounts, due to formation from the elemental sulphur by oxidation in presence of alkalies.

*Acid-Insoluble Ash.*—The ash was treated with a warm mixture of diluted hydrochloric acid, containing a little nitric acid, the insoluble material collected in a weighed Gooch crucible, washed with water, dried, heated to low redness, cooled and weighed. From 0.7190 Gm. of original material a weight of 0.0253 Gm. of acid-insoluble material was obtained, equivalent to 3.52 per cent. A duplicate of 2.1276 Gm. gave a weight of 0.0789 Gm., equivalent to 3.70 per cent. Average, 3.61 per cent. of acid-insoluble ash. Under the microscope the acid-insoluble material appeared to be talc.

*Calcium.*—The acid-soluble portion of the ash obtained as above was evaporated to small volume to remove most of the excess of acid, the solution diluted with water to a bulk of about 75 c.c. An excess of ammonium oxalate solution was added, the solution heated nearly to boiling and an excess of ammonium hydroxide added slowly. The mixture was kept hot for two hours and the bulk of the supernative liquid decanted through a filter. The precipitate was dissolved in a slight excess of warm, diluted hydrochloric acid and the calcium reprecipitated in the usual way. The precipitate was collected in a weighed Gooch crucible, dried and ignited at the low temperature and weighed as calicum carbonate. The residue obtained in this way was moistened with ammonium carbonate solution, dried and the residue again heated and weighed.

The calcium carbonate obtained from 0.7190 Gm. of material weighed 0.0817 Gm., equivalent to 4.54 per cent. of calcium. 2.1276 Gm. of material weighed 0.2351 Gm., equivalent to 4.41 per cent of calcium. Average, 4.49 per cent of calcium.

*Loss Over Sulphuric Acid.*—It was found that moisture could not be determined by drying at 100 C. because this treatment caused a steady loss, probably due to oxidation of the free sulphur. Therefore the loss by drying over sulphuric acid was determined. A weight of 2.1276 Gm. lost 0.0611 Gm. on drying over sulphuric acid for 48 hours. This is equivalent to 2.87 per cent. loss. A duplicate of 1.0575 Gm., lost 0.0296 Gm., equivalent to 2.80 per cent. Average, 2.84 per cent loss over sulphuric acid.

*Potassium and Sodium.*—Potassium and sodium were determined as mixed sulphates according to the method described in The Reports of the Chemical Laboratory, A. M. A. Vol. 6, 1913, p. 44. The mixed alkali sulphates from 1.6270 Gm. of material weighed 0.2000 Gm. and the barium sulphate obtained from this mixture weighed 0.2766 Gm. By calculation this is found to be equivalent to 0.59 per cent. of sodium and 4.68 per cent. of potassium. The mixed alkali sulphates from 2.1276 Gm. weighed 0.2596 Gm. and the barium sulphate obtained from this weighed 0.3608 Gm. By calculation these weights are equivalent to 4.56 per cent. of potassium and 0.67 per cent. of sodium. Average, 4.62 per cent of potassium and 0.63 per cent of sodium.

*Emodin-Bearing Drugs.*—The test for emodin-bearing drugs in San-Gri-Na was complicated by the presence of phenolphthalein. Some of the material was macerated with 1 per cent. sodium hydroxide solution and the mixture filtered. The filtrate was boiled for a few minutes. The red color disappeared, the remaining solution being pale yellow. This was taken to indicate the absence of free emodin. Another portion of the material was boiled in a reflux apparatus with 2 per cent. hydrochloric acid for 20 minutes. The mixture was filtered and shaken thrice with ether. The ether extracts were united, evaporated to dryness, the residue taken up with 1 per cent. sodium hydroxide and the solution boiled. The red color disappeared, the resulting solution being pale yellow. This was taken to indicate the absence of combined emodin complexes in San-Gri-Na.

## WELDONA FOR RHEUMATISM

(An answer to a query was published in *The Journal*, Dec. 13, 1924, p. 1943, based on the following preliminary report.)

Weldona is sold by the Weldona Co., of Boston. It is advertised for "Rheumatism of the joints, sciatica, lumbago, and rheumatic neuritis or muscular rheumatism."

The treatment consists of two kind of tablets. One consisted of three white tablets in an envelope which was labeled "Important. The tablets in this envelope are for constipation only." These laxative tablets were coated with calcium carbonate. The medicinal portion consisted essentially of an extract of an emodin-bearing drug probably cascara. Alkaloids and glycyrrhiza were absent.

The second portion of the Weldona Treatment consisted of sixty-five lavender colored tablets each coated with a mixture of calcium carbonate and sucrose (cane sugar). The medicinal portion was dissolved in water so far as possible, the extract filtered and the filtrate examined. Acetylsalicylic acid, alkaloids, sulphates, chlorides, and phosphates were absent. A salicylate and a sodium compound were present in considerable amounts. Also an extract from an unidentified vegetable drug was found. From the findings from these tests it appears probable that the chief antirheumatic constituent of Weldona is sodium salicylate.

## CARSINOL

*(Abstracted, with additions, from The Journal A. M. A., Jan. 17, 1925, p. 221)*

Carsinol, "the Personal Germicide," is marketed by the "Carsinol Research Laboratories," St. Joseph, Mo. In the advertising it is stated that "Carsinol is a new and novel germicide, developed through four years of diligent research," and that its chemical name is "ortho-phenol-mercuric-chlorate." In the information furnished the Council on Pharmacy and Chemistry, the following chemical formula is assigned to the preparation: $C_6H_4OH\ HgClO_3$. However, while these statements assert that Carsinol is a definite chemical substance, the Carsinol label contains the admission, probably in conformity with the requirements of the federal insecticide law, that the product contains "Inert ingredients: Water not over 88.03 per cent." In consideration of this discrepancy between the claims and the statement on the label, the Council requested the Laboratory to check the claims of composition.

Two original specimens of Carsinol (Carsinol Research Laboratories, Inc., St. Joseph, Mo.), were submitted to the A. M. A. Chemical Laboratory by the Council on Pharmacy and Chemistry. According to the label, Carsinol is an "odorless—stainless, non-poisonous, non-irritating" germicide. "Inert ingredients not over 88.03 per cent." In the information submitted, it was stated to be "ortho-phenol-mercuric-chlorate. $C_6H_4OH\ HgClO_3$." Each bottle contained about 190 cc. (approximately 6 fluid ounces) of a yellow liquid having a slightly alkaline reaction. Qualitative tests indicated the presence of sodium, mercury, chlorate, a substance resembling phenol and a small amount of chloride. Quantitative estimations yielded the following:

| | | |
|---|---|---|
| Specific gravity at 25 C | 1.083 | |
| Loss in weight at 100 C | 87.8 | per cent. |
| Sodium $(Na^+)$ | 2.53 | per cent. |
| Mercury $(Hg^{++})$ | 0.075 | per cent. |
| Chlorate $(ClO_3^-)$ | 9.19 | per cent. |
| Phenol-like substance (as phenol) | 0.02 | per cent. |

From the analysis, Carsinol is essentially a solution containing 11.7 per cent by weight of sodium chlorate, 0.01 per cent of mercuric chloride (1 part to 10,000 parts of water) and 0.02 per cent phenol (1 to 5,000). Assuming the product to contain 88 per cent water (as declared on the label), the amount of mercury present is approximately $^1/_{75}$ of that claimed according to the chemical formula submitted by the manufacturer, while there is four times as much chlorate ion $(ClO_3^-)$ present. The claimed composition for the product, therefore, is obviously false and misleading.

The advertising that accompanies the trade package contains misleading statements, such as these:

> "The odorless properties of CARSINOL makes its use ideal in contagious disease cases. Dip a large sheet in a 1% solution of CARSINOL (a 6-oz. bottle makes 4 gallons), and hang up in the sickroom. This causes the germs in the air to deposit on the sheet and lessens the danger of contagion."

This absurd claim has been criticized so frequently that its use by "Research Laboratories" is surprising.

> "Personal cleanliness, before the introduction of CARSINOL, was accomplished only at the risk of danger to life and tissues, intense irritation, and unpleasant odors. Bichloride of mercury, phenol and cresol compounds not only irritate the membranes of the body, but are also strong poisons."

In consideration of the report of the Laboratory, The Council declared that "these assertions cannot be accepted."

"Carsinol is indispensable for proper, safe personal hygiene." By statements such as these the promiscuous use of the vaginal douche is encouraged and the public invited to place false dependence on this "Personal Germicide."

The Council declared Carsinol inadmissable to New and Nonofficial Remedies because it is marketed under a false statement of composition and a nondescriptive name, and under unwarranted therapeutic claims that may lead the public to place dependence on it.

### Details of Analysis

*Loss in Weight.*—Twenty-five cc. of the original was evaporated to dryness on a steam bath. The weight of solids was 3.2992 Gm., equivalent to 87.8 per cent loss in weight.

*Ash.*—If the product was of the formula claimed (namely $C_6H_4OH\ HgClO$) there should be no ash. The solids from the foregoing determination were heated over a flame for 15 minutes. The residue weighed 2.5442 Gm., equivalent to approximately 9 per cent. It was quite evident, therefore, that the formula was fictitious. Qualitative tests indicated that ash was composed essentially of sodium chlorate and sodium chloride.

*Mercury.*—An aliquot of the original was diluted with about an equal volume of water and an equal volume of nitric acid in a pressure bottle which was then tightly sealed. The bottle was maintained at 100 C. for one hour, cooled, the liquid transferred to a platinum dish, diluted and electrolyzed for one hour. (a) Ten cc. yielded 0.0083 Gm. of mercury, equivalent to 0.076 per cent. (b) Ten cc. yielded 0.0081 Gm. of mercury, equivalent to 0.075 per cent.

*Chlorate.*—An aliquot of the original was transferred to 150 cc. beaker, 10 cc. of hydrochloric acid was added and the solution heated on the steam bath to dryness. Then 5 cc. of water and 5 cc. of hydrochloric acid was added and evaporated again to remove chlorine ($Cl^-$). The residue was then taken up in water, transferred to a platinum dish, evaporated to dryness on a steam bath, heated for two hours in an oven at 120 C. and finally over a free flame, care being taken not to lose any material by either decrepitation or excess heat. (a) Ten cc. yielded 0.6994 Gm. of sodium chloride, equivalent to 9.21 per cent of chlorate ($ClO_3^-$). (b) Ten cc. yielded 0.6957 Gm. of sodium chloride, equivalent to 9.17 per cent chlorate ($ClO_3^-$). Average, 9.19.

*Sodium.*—The residue weighed as sodium chloride (a) in the foregoing was heated with diluted sulphuric acid, and carefully evaporated to dryness. It was heated over a free flame until the normal sulphates remained, cooled and weighed. The residue from (a) of the foregoing weighed 0.8490 Gm., equivalent to 2.54 per cent sodium ($Na^+$). The sodium chloride (b) was calculated to sodium, which was equivalent to 2.53 per cent sodium ($Na^+$).

*Phenol.*—An aliquot of the original and 1 Gm. of sodium bicarbonate were transferred to a steam distillation flask (as described in Methods of Analysis, A. O. A. C. 2nd ed. revised to July 1, 1924, p. 365) connected on the intake with a source of washed carbon dioxide, and to the condenser on the output. The phenol and water from the steam distillation was collected until 200 cc. had passed over. The phenol was titrated according to method of assay of U. S. P. IX, p. 317. (a) Ten cc. consumed 1.47 cc. of tenth normal potassium bromide-bromate, equivalent to 0.021 per cent of phenol. (b) Ten cc. consumed 1.37 cc. of tenth normal potassium bromide-bromate, equivalent to 0.019 per cent phenol.

## BETO

### Epsom Salt Fraud Sold as Cure for Diabetes

*(Abstracted from The Journal A. M. A., Jan. 24, 1925, p. 304)*

"Beto" is advertised as a "Blessing to Diabetics." It was put on the market originally by one John Baring of Chicago. Baring died in September, 1924, but the nostrum is still exploited, and letters that go out are still signed "John Baring." Like most nostrums sold for the alleged cure of diabetes, Beto is featured as a product whose use makes it unnecessary for the diabetic to diet; as the advertisements say: "Absolutely no dieting." The prospective purchaser is told that if he takes Beto he can eat just as he has been accustomed to. When first put on the market, Beto was sold and advertised exclusively as a cure for diabetes. Today it is recommended, in addition, for high blood pressure, "all kidney troubles" and dropsy.

The selling story for Beto is typical of "patent medicine" exploitation. Baring claimed that he suffered from diabetes for eighteen years and medical science gave him no help, but that he became weakened, emaciated and threatened with gangrene. Then, said Baring:

> "I made the lucky discovery in the shape of a medical preparation with which I had been experimenting for a long time and found that I had discovered the only successful method of eliminating diabetes."

Because of the number of inquiries received regarding this product and the dangerous possibilities in its sale, it was decided to analyze Beto and give the medical profession and the public the facts regarding it. One package of Beto sells for $5. A package was purchased and turned over to the A. M. A. Chemical Laboratory.

One original box of "Beto" (John Baring, 736 Lotus St., Chicago) was submitted to the Laboratory for examination. The box contained 100 large white tablets, having an average weight of 7.3 grams (approximately ¼ oz.) each. The powdered material possessed an odor resembling oil of cinnamon. Qualitative tests indicated the presence of talc, magnesium, a trace of sodium and sulphate. Alkaloids, sugars, emodin-bearing drugs, and vegetable drugs or extracts were not found. On heating the product in an oven at 160 C. for two hours, it lost 40 per cent in weight, and at 225 to 250 C. it lost 48 per cent in weight. This is characteristic of magnesium sulphate hydrated (Epsom salt). Quantitative determinations were as follows:

| | |
|---|---|
| Acid-insoluble material (talc) | 2.8 |
| Magnesium ($Mg^{++}$) | 9.7 |
| Sulphate ($SO_4^{--}$) | 39.1 |
| Water of crystallization (by difference) | 48.4 |
| | 100.0 |

The product, therefore, may be considered to have essentially the following composition:

| | |
|---|---|
| Talc | 3 per cent. |
| Magnesium sulphate, U. S. P. (Epsom salt) | 97 per cent. |
| Oil of cinnamon | trace |

Each tablet is equivalent to approximately 7 grams of Epsom salt, or one-half the dose for magnesium sulphate as given in the U. S. Pharmacopeia.

In commenting on this, THE JOURNAL stated:

"It will thus be seen that the purchaser of a five dollar package of Beto gets 1½ pounds of Epsom salt for his money. A good grade of medicinal Epsom salt can be bought at retail for less than 15 cents a pound. Here we have a good example of the point that the Pure Food and Drugs Act needs an amendment. Did the law abolish secrecy of composition in the sale of home remedies, how many people could Baring persuade to pay $5 for 25 cents worth of Epsom salt? More important still, had the public known that Beto is nothing more mysterious than Epsom salt, how many diabetics would have ever purchased the stuff in the belief that they were going to be cured by this preposterous piece of quackery?

"When THE JOURNAL occasionally emphasizes the discrepancy between the selling price of a nostrum and the price of the ingredients of that nostrum, the 'patent medicine' interests retort that such comparisons are unfair. In the case of meritorious merchandise, it is perfectly true that it is unfair to compare the selling price of such merchandise with the cost of raw materials. In the case of nostrums, however, this does not hold. The 'patent medicine' people themselves have admitted that one half of their receipts go for newspaper advertising alone—to say nothing of the vast sums spent on 'almanacs,' window displays, circulars and other publicity features. From the same source—the nostrum exploiters—has come the admission that at least three out of every four who purchase 'patent medicines' are hypochondriacs who merely *think* that they are suffering from the ailments the nostrums are supposed to cure. When John Doe pays a dollar for a bottle of Dr. Quack's Panacea he little realizes that from fifty cents to seventy-five cents of the dollar has been expended in an effort to convince him that he suffers from the conditions for which Dr. Quack's Panacea is recommended. With such an enormous overhead—one that no legitimate business could maintain—no wonder Dr. Quack finds it necessary to charge a dollar for that which costs him less than five cents. When a concern, as in the present instance, sells as a cure for diabetes a quarter's worth of Epsom salt for five dollars and markets this in such a way that the public has no idea as to what it is buying there is ample justification for directing attention to the difference between the cost of ingredients and the selling price.

"Beto is not a cure for diabetes, and to sell Epsom salt under the claim that it is a cure, and with the deadly dangerous advice that when taking it it is unnecessary for the diabetic to diet, is an offense against business morals and a menace to the public health."

### Details of Analysis

*Loss in Weight.*—It is difficult to make exact determinations of water of hydration in magnesium sulphate as it requires a temperature above 200 C. to remove it, and at this temperature there may also occur a slight decomposition of the anhydrous salt; thus exact quantitative results by this method may not be obtained easily. At about 150 C. magnesium sulphate loses approximately 43 per cent of its weight. In order, therefore, to determine if the difference between the quantitative determinations for talc, magnesium and sulphate and 100 per cent was due to water of hydration, the powder was heated at these two temperatures. As a result it was concluded that the magnesium sulphate was present in the hydrous form as the loss in weight was about equal to the magneisum sulphate (as anhydrous) present. This is in accordance with the standards for magnesium sulphate U. S. P. (a) 1.1236 grams was dried at 160 C. for $2\frac{1}{2}$ hours; the loss in weight was 0.4494 gram, equivalent to 40.01 per cent; on further heating at 225 to 250 C. for 4 hours, the loss in weight was 0.5362 Gm., or 47.7 per cent. (b) 1.1520 Gm. was heated at 160 C. for $2\frac{1}{2}$ hours; the loss in weight was 0.4543 Gm., equivalent to 39.43 per cent. On further heating at 225 to 250 C. for four hours the loss in weight was 0.5491 Gm., equivalent to 47.6 per cent.

*Insoluble Material.*—The insoluble material was filtered from the solution used for magnesium determinations, washed, ignited in tared platinum crucible and weighed. (a) 1.0844 Gm. yielded 0.0298 Gm. of insoluble material, equivalent to 2.74 per cent. (b) 1.3774 Gm. yielded 0.0388 Gm. of insoluble material, equivalent to 2.80 per cent.

*Magnesium* ($Mg^{++}$).—The filtrate from the insoluble material was used for the magnesium determination. The method employed was that described in the U. S. Pharmacoepia IX under magnesium sulphate. (a) 1.0844 Gm. yielded 0.4800 Gm. of magnesium pyrophosphate, equivalent to 9.68 per cent magnesium ($Mg^{++}$). (b) 1.3774 Gm. yielded 0.6104 Gm. of magnesium pyrophosphate, equivalent to 9.67 per cent magnesium.

*Sulphate.*—A weighed sample was dissolved in water, the insoluble material filtered off and washed well; the filtrate was treated in usual manner with barium chloride solution in presence of a small amount of hydrochloric acid. (a) 0.7701 Gm. yielded 0.7311 Gm. of barium sulphate, equivalent to 39.06 per cent sulphate ($SO_4^{=}$). (b) 0.6042 Gm. yielded 0.5756 Gm. of barium sulphate, equivalent to 39.19 per cent sulphate ($SO_4^{=}$).

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## KARNAK

### Another Anti-Volsteadian Nostrum

*(Abstracted, with additions, from The Journal A. M. A., Feb. 7, 1925, p. 460)*

"Karnak" (Drug Products, Inc., Atlanta, Ga.), admittedly contains 18 per cent of alcohol by volume. What is not admitted is the fact, to be shown later, that it does not contain enough drugs of sufficient potency to prevent its use as a beverage. The individuals who are back of the Karnak outfit seem to be experts in the exploitation of alcoholic nostrums, for it appears that before floating Karnak they were employed by the Tanlac concern and before that by the company that puts out Wine of Cardui. With such an array of experience and talent behind it, Karnak will doubtless be a great seller.

Some of the claims made for Karnak in the newspaper advertisements, where falsehood is free from penalties, are that it "contains no powerful drugs that only deaden the pain for awhile." The stuff is said to be prescribed and praised by "one of New York's most eminent specialists"! According to the statements on, or in, the trade package, Karnak is "composed of nine of the most beneficial roots, barks and herbs known to medical science." It is "purely vegetable and free from injurious or habit-forming drugs." Analysis shows, as will be brought out later, that the chief therapeutically active drug in Karnak is alcohol, of which there is twice as much as there used to be in champagne. To say that a product whose essential ingredient is alcohol is not "habit-forming" is to deny one of the best established facts of human experience. Yet this statement is made on the trade package of Karnak, a fact that is respectfully brought to the attention of the Department of Agriculture.

### THE MYTHICAL "NOTED FRENCH CHEMIST"

In the introductory advertising campaign of Karnak, the statement is made and featured that the product was "discovered by M. Pierre Andre, noted French chemist." No such statement as this appears on or in the trade package, which is subject to the control of the federal Food and Drugs Act. The statement appears only in the newspaper advertisements. Correspondence with those in French scientific circles brought the not unexpected statement that there is no noted French chemist by the name of Pierre Andre.

Karnak was extensively advertised in newspapers. Following the sensational three column advertisements which constituted the opening guns of the Karnak advertising campaign, there came a series of advertisements of the classic testimonial type. They could be calculated to keep the product before the attention of those who were looking for something in this line. A study of the testimonials shows a similarity of style that causes one to wonder whether Drug Products, Inc., has a standard form for its devotees to sign. Thus, Mrs. Prettyman of Kansas City suffered from gas on the stomach so that she could hardly breathe; Mr. Bucher of Kansas City would "bloat up as tight as a drum," and Mr. Reeves of Wichita said food "would bloat me up with gas as tight as a drum;" all used Karnak, and the bloating ceased. Mr. Durham of Kansas City suffered from indigestion and nervousness, as did also Captain Chellew, until some one brought Karnak to their attention; the captain now eats like a farm hand. Mr. Frank Crites had indigestion and stomach trouble with gas pains and headaches, but after taking Karnak he never felt better in his life. It is difficult to conceive the mental processes of people who will accept testimony of this sort, but the millions spent by nostrum exploiters in giving publicity to these testimonials demonstrate that such testimony is accepted.

Two original bottles of Karnak (Drug Products, Inc., Atlanta, Ga.) were submitted to the Laboratory for examination. Each bottle contained approximately 7½ fluidounces of a brownish-red liquid having an aromatic odor, and at first a sweetish, licorice-like, afterward mildly bitter, taste. In the circular accompanying the trade package, the claim is made that the preparation is "purely vegetable" and composed of "nine of the most beneficial roots, barks, and herbs known to medical science." The name of none of the nine drugs was given. The label on the bottle declared the presence of 18 per cent of alcohol by volume.

Qualitative tests indicated the presence of alcohol, ammonium ($NH_4^+$), glycyrrhiza (licorice), emodin-bearing drugs, reducing sugars and small amounts of calcium and magnesium. A trace of a substance responding to the usual alkaloidal reactions was detected, but not identified. Tests for quinine, caffeine, strychnine, hydrastine, brucine and berberine (drugs sometimes employed as so-called "tonics") were negative. Other than licorice and an emodin-bearing (laxative) drug, no other vegetable extractives were identified.

Quantitative determinations yielded the following results:

| | | |
|---|---|---|
| Specific gravity at 25 C./25 C. ........ | 1.019 | |
| Alcohol ........................... | 15.56 | per cent. by volume |
| Solids ............................ | 10.036 | gm. per 100 c.c. |
| Ash ............................... | 0.244 | gm. per 100 c.c. |
| Total anthraquinones (Daels' method).. | 0.132 | gm. per 100 c.c. |
| Total alkaloids ...................... | 0.008 | gm. per 100 c.c. |
| Glycyrrhizic acid (from licorice)....... | 0.55 | gm. per 100 c.c. |

While the Daels' method for the assay of emodin-bearing drugs has been criticized as not affording an accurate gage of the laxative value of these drugs, it still remains as the best approximation to their value of any chemical method known. According to the results obtained by this method, Karnak does not represent more than about 10 per cent of aromatic fluidextract of cascara. The results from the assay of the preparation for glycyrrhizic acid indicate about 5 per cent of fluidextract of glycyrrhiza.

In order to determine whether or not the preparation possessed marked laxative or other physiologic effects, 60 c.c. (2 ounces, or four doses, equivalent to the amount recommended daily) were diluted with 60 c.c. (2 ounces) of water, the mixture evaporated to the original volume to remove alcohol, and the residue swallowed at one dose by an adult. The result was negative. The foregoing evidence indicates that Karnak contains no active drugs in sufficient amounts to produce physiologic effects in ordinary doses.

In view of these findings, the Chemical Laboratory obtained the aid of Dr. Hugh McGuigan, head of the department of pharmacology of the University of Illinois. A number of original specimens of Karnak, purchased in the open market, were used by Dr. McGuigan to determine its pharmacologic action. In due time Dr. McGuigan reported:

> Tests of the samples of Karnak show that this concoction is not sufficiently medicated to prevent its use as a beverage. This conclusion is based on its action on men and on a dog. Four men ("A," "B," "C" and "D"), varying in ages from 19 to 50 years, took divided doses of Karnak within two and one-quarter hours as follows:
>
> "A": 19 yrs.; wt., 156 lbs. Three doses of 30 c.c. (1 oz.) each; total 90 c.c. (3 oz.).
>
> "B": 50 yrs.; wt., 175 lbs. Three doses of 30 c.c. (1 oz.) each; total 90 c.c. (3 oz.).
>
> "C": 22 yrs.; wt., 220 lbs. Four doses of 60 c.c. (2 oz.) each; total 240 c.c. (8 oz.).
>
> "D": 35 yrs.; wt., 175 lbs. One dose of 220 c.c. (7⅓ oz.).
>
> There was some alcoholic effect with these doses, varying from flushing of the face to slight incoordination. No other effect was observed or produced except that with the largest dose — a whole bottleful—there was a slight laxative action.
>
> A dog, weighing 7 kg., was given by stomach 163 c.c. from which alcohol had been evaporated on a water bath. There was no effect except a weak laxative action. Three days later this dog was given 2 c.c. fluidextract cascara sagrada (Lilly) followed by 100 c.c. water. This elicited six observed bowel movements of a thin consistency.
>
> Three of the men who had taken Karnak took doses of the aromatic fluidextract of cascara sagrada (Fuller-Morrison) as follows: 10 c.c. (about 2.7 fl. dr.), 15 c.c. (about ½ oz.) and 25 c.c. (about ¾ oz.), respectively. The 10 c.c. dose caused a very slight laxative action, while the two larger doses caused brisk catharsis.
>
> The laxative action of Karnak, therefore, is considerably less than one-tenth the volume of the aromatic cascara. From a knowledge of the action of cascara, I am of the opinion that an entire bottle of Karnak does not contain the cathartic equivalent of 2 c.c. (about 32 minims) of the fluidextract of cascara.

Thus, both the chemical and the pharmacologic reports show that Karnak is not sufficiently medicated to prevent its use as a beverage.

The JOURNAL commented on the product as follows:

"In view of the findings, THE JOURNAL feels justified in asking: What is the Internal Revenue Department going to do about it? Another point of interest: Certain states, independent of federal action, prohibit physicians from prescribing wine or whisky even under the restrictions imposed by the federal laws. Yet, apparently, the same states permit without let or hindrance the unrestrained sale of nostrums whose chief ingredient is alcohol and that are not sufficiently medicated to prevent their use as beverages."

### Details of Analysis

*Specific Gravity.*—The specific gravity was taken with a pycnometer at 25 C. compared with water at 25 C. The specific gravity found was 1.0191 at 25 C./25 C.

*Total Solids.*—Total solids were determined by drying a measured volume of the preparation in a weighed dish on the steam bath and afterward drying the residue at 100 C. Ten c.c. of the material gave a residue weighing 1.0057 Gm., equivalent to 10.07 Gm. per 100 c.c. A duplicate of 10 c.c. gave a residue weighing 1.0006 Gm., equivalent to 10.01 Gm. per 100 c.c. Average, 10.04 per 100 c.c.

*Ash.*—Ash was determined by heating the residue obtained by drying the material at 100 C. to a low red heat until the residue was carbonized and most of the carbon had been burned away. The residue was moistened with water, dried and again heated until constant weight had been attained. The ash from 10 cc. weighed 0.0247 Gm., or 0.2470 Gm. per 100 cc. A duplicate of 10 cc. gave 0.0253 Gm. of ash, or 0.2530 Gm. per 100 cc. Average, 0.244 Gm. of ash per 100 cc.

*Alcohol.*—Alcohol was determined by the A. O. A. C. method. 100 cc. of the original was distilled to 100 cc. at 15.6 C. The distillate was sufficiently clear not to require shaking with petroleum benzin. The distillate weighed 24.5336 Gm. as compared with a weight of 25.0200 Gm. for the same volume of water. This is equivalent to a specific gravity of 0.98056 at 15.6 C. or 15.56 per cent of alcohol by volume. The label declares the presence of 18 per cent. of alcohol.

*Total Alkaloids.*—A measured portion of the solution was slightly acidified with diluted sulphuric acid and the mixture evaporated to half the original volume to remove alcohol. The residue was made alkaline with ammonia water and the solution repeatedly shaken with 15 cc. portions of chloroform until all of the alkaloid had been removed. The bulked chloroform solution was repeatedly shaken with very dilute hydrochloric acid until all of the alkaloid had been removed from the chloroform. The acid layers were united, the solution washed once with 10 cc. of chloroform, the solvent discarded, the acid solution made alkaline with ammonia water and the solution shaken with 25, 15 and 10 cc. of chloroform respectively. The several portions of solvent were united, the solution washed once with water and the washed solution evaporated by means of a fan and gentle heat. The residue was dried at 100 C. for 10 minutes and weighed. The alkaloid from 100 cc. of the original material weighed 0.0079 Gm. This is equivalent to about 0.0036 grain per fluid ounce of original material. The alkaloid did not respond to tests for any of the common potent alkaloids used in medicine, such as morphine, strychnine, quinine, atropine, hydrastine, colchicine, caffeine, berberine or brucine.

*Total Anthraquinones.*—The method used for estimating the total anthraquinones was essentially that of Daels[1]. As used in this examination the method is as follows:

> Dealcoholize 50 cc. of the preparation by dilution with 50 cc. of water and evaporate in a beaker on the water bath to a volume of 50 cc., transfer the residue to an Erlenmeyer flask of 500 cc. capacity using a few cc. of water and 50 cc. of 25 per cent sulphuric acid, and if necessary, a few drops of ammonia water to rinse the container. Add 200 cc. of chloroform, attach to a reflux condenser, immerse the bottom of the Erlenmeyer flask in a water bath and heat to the boiling point of chloroform for 2½ hours.. Allow the flask to cool and transfer the contents to a separator, washing out the flask with a little fresh chloroform. Draw off the chloroformic solution into another Erlenmeyer flask. Add 50 cc. of chloroform to the acid mixture in the separator, shake thoroughly and after separation has taken place, draw off the chloroformic solution and add it to the portion previously collected. Shake again with 25 cc. of chloroform and add the solvent to the previous extracts. Discard the acid mixture. Recover about 2/3 of the chloroform by distillation and pour the balance into a separator, washing thoroughly with fresh chloroform to remove final traces of anthraquinone derivatives. Agitate the chloroform solution. with 25 cc. of 10 per cent sodium hydroxide, draw off the chloroform and subject it to another shaking treatment with 10 cc. of 10 per cent sodium hydroxide diluted with 15 cc. of water. Draw off the chloroform and wash it with 25 cc. of water, adding the wash water to the united sodium hydroxide solutions. A fourth and a fifth shaking with dilute sodium hydroxide may be necessary if the alkaline solution from the third shaking is colored pink. Add an excess of hydrochloric acid to the alkaline mixture and shake out three times with 25, 15 and 10 cc. of chloroform, respectively. A fourth and fifth shaking with

> chloroform may be necessary if the third chloroformic extract is colored more than faintly yellow. Discard the acid layer and wash the bulked chloroform solution by shaking with 50 cc. of water. Allow to separate completely, filter the chloroform through cotton into a tared Erlenmeyer flask and recover the solvent by distillation. Add 1 cc. of alcohol to the residue, evaporate on the steam bath, dry the residue at not over 100 C. for 30 minutes, cool in a desiccator and weigh. The weight represents the total anthraquinone bodies in 50 cc. of the preparation.*

The total anthraquinones from 50 cc. of original material weighed 0.0685 Gm., or 0.1370 Gm. per 100 cc. A duplicate of 50 cc. gave 0.0636 Gm. of total anthraquinones, or 0.1272 Gm. per 100 cc. Mean 0.1324 Gm. per 100 cc. Assuming that a well made fluid extract of cascara should yield about 1.5 Gm. of total anthraquinones per 100 cc. Karnak does not represent more than about the equivalent of 11 per cent of fluid extract of cascara.

## ASPATOL

*(Abstracted, with additions, from The Journal A. M. A., Feb. 14, 1925, p. 533)*

Aspatol is sold by the Standard Chemical Company, Des Moines, Iowa, as representing "in pleasant and permanent form and in special combination, forty grains of the soluble salt of Acetylsalicylic Acid per fluid ounce." According to the label "This preparation tends to avoid gastric and intestinal irritation, nausea, restlessness, and such unpleasant results as may develop from the use of other Salicylates."

Some time ago an inquiry was received which referred to the claims made for Aspatol, asking whether or not it is possible to incorporate acetylsalicylic acid or any salt of this substance in liquid form without decomposition occurring. Ever since acetylsalicylic acid (aspirin) has been in popular vogue, some firm or other has endeavored to dispense it in liquid form. A number of years ago pharmaceutical magazines were giving out information as to how a "stable" solution of acetylsalicylic acid could be prepared by dissolving the acetylsalicylic acid in a rather strong sodium citrate solution. At that time the A. M. A. Chemical Laboratory[1] showed that when such a solution was prepared, the acetylsalicylic acid broke down, as was to be expected, so that after seventeen days a patient taking such a solution was in reality taking the equivalent of sodium salicylate—with all its advantages and disadvantages. In fact, such a preparation was 75 per cent. decomposed in that time and was far from being a "stable" solution. Notwithstanding this added evidence of the instability of acetylsalicylic acid in water, the Des Moines "Standard Chemical Company" makes the claim that their preparation does not break down. For instance, in a letter sent out by the concern, signed by F. A. Mallett, *Factory Superintendent* [italics ours] the following statement occurs:

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* In extracts that contain much resinous matter or substances, precipitable by acids, such as glycyrrhiza, it may be found advisable after the first three extractions with chloroform to filter the acid mixture through a Gooch crucible containing asbestos in order to collect as much of the precipitate as possible. The precipitate remaining in the original Erlenmeyer flask and that in the separator, if any, is washed with water. All of the precipitate is then dissolved in a few cc. of 10 per cent sodium hydroxide and the acid filtrate added to the solution. Fifty cc. of the chlororform and 10 cc. of 25 per cent sulphuric acid are added to the alkaline mixture and the mixture refluxed at the boiling point of chloroform for two hours. The mixture is cooled, placed in a separator and the chloroform layer added to the bulked chloroform from the first extraction. The acid layer is washed with 20 cc. of chloroform and the solvent added to the principal extract. The extraction of the anthraquinones is then carried out in the usual way by solution in diluted sodium hydroxide solution and subsequent extraction with chloroform from an acid medium.

> "Aspirin, or Acetyl Salicylic Acid, as you know, Doctor, is almost insoluble in water, or syrup, so to make a soluble Aspirin preparation, it is necessary to convert the Acetyl Salicylic Acid into a soluble salt. This we do by our special process; thus making an Acetyl-Salicylate which is soluble in syrup base.
>
> "Hence, our preparation really does contain Aspirin, combined as an Acetyl Salicylate, which is the only water soluble form.
>
> "This preparation, sometimes called "Soluble Aspirin," is being used by a great number of physicians where Aspirin is indicated and in many cases they prefer the pleasant quick-acting soluble salt to the tablet."

As such claims concerning the stability of the preparation seemed unlikely, the A. M. A. Chemical Laboratory investigated the product.

One original specimen of Aspatol was obtained from the Standard Chemical Company of Des Moines, Ia., and the contents submitted to examination. The bottle contained one pint of a syrupy liquid having an aromatic odor and a reddish-orange color. Qualitative tests indicated the presence of calcium, a very small amount of acetylsalicylate, considerably larger amounts of salicylate, acetate and invert sugar. Quantitative determinations yielded the following:

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[1] Leech, P. N.: Acetylsalicylic Acid in Sodium Citrate Solution, J. A. M. A. **78**: 275 (Jan. 28) 1922.

| | |
|---|---|
| Specific gravity (at 25 C.) | 1.18 |
| Acetylsalicylic acid | 0.71 per cent. |
| Salicylate (as salicylic acid) | 3.83 per cent. |
| Calcium ($Ca^{++}$) | 0.95 per cent. |
| Invert sugar | 14.06 per cent. |
| Ash | 1.38 per cent. |

From the foregoing, it is concluded that the solution was probably prepared from calcium acetylsalicylate, but as was expected it had been decomposed. The amount of acetylsalicylate present represented only about 12.41 per cent. of the original acetylsalicylic acid (as calculated from the quantitative estimations).

Thus each dose (one teaspoonful) of Aspatol may be considered to contain essentially acetylsalicylic acid 0.034 Gm. (about ½ grain); salicylic acid in the form of both free salicylic acid and salicylates equivalent to 0.20 Gm. (3 grains) and calcium salicylate with some calcium acetate in a syrupy solution. From a chemical standpoint this preparation has no advantages over the well-known salicylates.

In concluding its report, the Council on Pharmacy and Chemistry stated:

"The work again points out that acetylsalicylic acid and its salts are not stable in aqueous solutions, and physicians should bear this incompatibility in mind when importuned by advertisements or detail men to employ aqueous solutions of acetylsalicylic acid (aspirin).

"The Council declared Aspatol (Standard Chemical Company, Des Moines, Iowa) unacceptable because its composition is not correctly stated; the claims made for it are unwarranted, and the name is not descriptive of its composition."

### Details of Analysis

*Salicylic Acid, Acetyl Salicylic Acid and Unhydrolyzed Acetyl Salicylic Acid.*—These determinations involve extraction and titration of the acids, hydrolysis with a known excess of sodium hydroxide of any acetyl compounds and the back titration of the remaining excess of sodium hydroxide. This procedure was carried out on the acids extracted from the untreated Aspatol solution and on the acids extracted from the same Aspatol solution acidulated with hydrochloric acid for two reasons. 1. The fact that acids can be extracted from Aspatol is proof either that the solution was not carefully neutralized or that hydrolysis had taken place. 2. No claim could be made that the hydrochloric acid added for the extraction was the cause of all of the hydrolysis. The determinations were carried on as follows:

> Accurately weighed samples of the syrup were extracted four times with ether using 30 cc., 25 cc., 20 cc., and 20 cc., portions. The ether was evaporated and the residue titrated in the presence of 10 cc. alcohol with standard tenth normal sodium hydroxide, using phenolphthalein as an indicator. A known excess of standard tenth normal sodium hydroxide was then added. The flask was heated on the steam bath for an hour, whereupon it was cooled and the remaining excess alkali titrated back with standard tenth normal hydrochloric acid.
>
> To the ether extracted syrup was added 10 cc. diluted hydrochloric acid and it was then re-extracted four times with ether using 30 cc., 25 cc., 20 cc. and 20 cc. portions. The ether was evaporated and the extract titrated exactly as described above.
>
> A sample of pure acetylsalicylic acid after similar treatment with hydrochloric acid showed far less hydrolysis. A sample of freshly prepared calcium acetylsalicylate showed more hydrolysis than the free acid but less than Aspatol.

*Calcium.*—Calcium was determined in three ways. (a) 5.2543 grams of the original was ashed. The residue was taken up in diluted hydrochloric acid and diluted to 250 cc. A 50 cc. portion of this solution was diluted to 100 cc. and then diluted ammonia water was added. The calcium was precipitated with ammonium oxalate solution. The solution was filtered and washed with water. The precipitate was dissolved in diluted hydrochloric acid and reprecipitated as described above. The precipitate was thrown on a prepared Gooch crucible and washed carefully. It was dried carefully in the oven at 100 C. and then it was heated in the full heat of the Meeker burner for two hours. It was cooled in a soda-lime desiccator and weighed as calcium oxide ($CaO$). There was no appreciable loss on further heating. The weight of the calcium oxide was 0.0143 gram. This represents 0.97 per cent calcium.

(b) To 5.3495 grams of the original in a platinum dish was added 5 cc. of sulphuric acid. The dish was heated over a steam bath until the material was well charred and then carefully over a low flame. Then the carbon was burned out with the full flame of the Bunsen burner. After cooling the ash was moistened with a drop of sulphuric acid. After gentle ignition the dish was cooled in a dessicator and weighed. The

## RECORD OF TITRATIONS

| Weight in Grams | Titration Cc. of N/10 NaOH | | Excess Cc. of N/10 NaOH | | Back Titration Cc. of N 10 HCl | | Salicylic Acid | | | | | Acetylsalicylic Acid | | | | | Per Cent of Original Acetyl-salicylic Acid Left Unhydro-lyzed |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | A | | B | | | A | | B | | | |
| | A † | B ‡ | A | B | A | B | Weight | Per Cent | Weight | Per Cent | Total per Cent | Weight | Per Cent | Weight | Per Cent | Total per Cent | |
| Aspatol 13.4408 | 7.55 | 36.56 | 5.73 | 28.42 | 4.02 | 24.28 | 0.0806 | 0.59 | 0.4476 | 3.33 | 3.92 | 0.0309 | 0.23 | 0.0745 | 0.55 | 0.78 | 13.70 § |
| Aspatol 13.0910 | 7.46 | 32.84 | 11.06 | 8.50 | 8.87 | 5.89 | 0.0727 | 0.55 | 0.4174 | 3.18 | 3.73 | 0.0394 | 0.30 | 0.0400 | 0.35 | 0.65 | 12.21 § |
| Acetyl * Salicylic Acid 0.5 | 28.05 | ..... | 29.40 | ..... | 7.98 | ..... | 0.0015 | .... | ...... | .... | .... | 0.3857 | .... | ...... | .... | .... | 77.15 |
| Acetyl Salicylic Acid 0.5 | 27.77 | ..... | 31.09 | ..... | 6.28 | ..... | 0.0418 | .... | ...... | .... | .... | 0.4468 | .... | ...... | .... | .... | 89.36 |

* Neutralized with calcium hydroxide ($Ca(OH)_2$).
A † Means first ether extract (before addition of acid).
B ‡ Means second ether extract (before addition of acid).
§ Average 12.95. The value calculated from the dosage figures is 12.41.

weight of the residue was 0.1783. This represents 0.98 per cent calcium ($Ca^{''}$).

(c) 2.8034 grams of the original was diluted with 15 cc. of water; 100 cc. of alcohol was then added and then sufficient water with stirring to dissolve any precipitate. The calcium was precipitated with 10 cc. of dilute sulphuric acid and the beaker set aside over night. The precipitated calcium sulphate was thrown on a Gooch filter, dried at 100 C. and weighed. The calcium sulphate weighed 0.0816 gram. This represents 0.92 per cent calcium ($Ca^{''}$).

*Invert Sugar.*—Polariscopic readings gave no appreciable amount of sucrose. 9.8368 grams of the original was diluted to 100 cc. To 10 cc. of the solution approximately 40 cc. of water was added, and 25 cc. of each of the Fehling solutions were added. The beaker was covered with a watch glass and heated to boiling, the heating taking approximately four minutes. The solution was boiled two minutes, filtered into a Gooch crucible while hot, washed with hot water, alcohol and finally ether. After drying at 100 C. for one hour the crucible was allowed to cool in a desiccator and weighed. The weights of cuprous oxide ($Cu_2O$) were: (a) 0.2945 gram and (b) 0.2939 gram. These amounts correspond to 1.3840 grams of invert sugar. This amounts to 14.06 per cent (Food Inspection and Analysis. Leach, fourth edition, page 622).

*Ash.*—A sample of Aspatol weighing 11.2350 grams gave 0.1552 gram of ash. This represents 1.38 per cent.

## BEFSAL

### Another Alleged Synthetic

*(Abstracted, with additions, from The Journal A. M. A., Feb. 21, 1925, p. 611)*

A number of inquiries have been received concerning a preparation widely circularized to physicians under the name "Befsal." One correspondent, a dean of a college of pharmacy, writes:

"Many local physicians have evidently been detailed about the following preparation, and are asking the drug stores what they know about it. They give the chemical name as dibenzyl-diethyl-methylene-disalicylic-dipyruvic (cinchoninic) acid. It was mentined in some paper written by Dr. Lambert Ott of Philadelphia. I wrote to Dr. Ott about it and he wrote back, giving me the trade names for it as Befsal and Pyrazo-phen. He also stated that he was getting out an Iodo-befsal. His reply was a form letter much in the nature of advertising. The preparations are used for rheumatism. He sent along an outlined treatment and diet which in detail should cure the rheumatism without the Befsal."

A physician from South Dakota inquires:

"Can you give me a line on Befsal as put out by Synthetic Organic Products Co., Inc., New York? They seem to make quite some claims for their products."

A physician from Connecticut writes:

"I would be greatly obliged to you if you would give me any information on a new compound named Befsal put up by Dr. Summers."

And from Colorado:

"The enclosed reprint came to my desk and never having heard of the drugs mentioned I wrote for further information and received the enclosed letter yesterday. It looks 'fishy," so I am writing you for a report on the doctor and his wonderful drugs."

Befsal seems to be exploited from two sources: Dr. S. Lewis Summers, Fort Washington, Pa., and the Synthetic Organic Products Co., New York City. Each exploiter gives an alleged formula for the product, but the two formulas are totally dissimilar. Two years ago Dr. S. Lewis Summers, "Producer of Synthetic Organic Chemical Compounds," was selling it under the chemical name dibenzyldiethylmethylenedisalicylic-dicinchoninic acid (whatever that means) with the formula $C_{30}H_{26}O_{10}$. In another advertisement Dr. Summers called the product "the Chinchoninic Acid and Benzylester Compound of A-F-Sal."

The Synthetic Organic Products Co., Inc., of New York (president: Joseph C. Richard) sends out circular letters that are practically the same as those sent out by Dr. Summers. This form gives the same type of ambiguous chemical name to Besfal as that given by Summers, but the formula, as given on the label, is quite different, namely $C_{55}H_{42}O_{10}N_2$.

The preparation is extensively puffed by Lambert Ott, M.D., who, a number of years ago, sang the praises of A-F-Sal. In reply to an inquiry, Dr. Ott (in a circular letter) states that Befsal can be obtained from C. A. Harold, a pharmacist in Philadelphia; he speaks of the product as the "benzyl ethyl esters of pyruvic acid compound of methylene disalicylic acid."

It may be recalled that fifteen or more years ago S. Lewis Summers was piloting the Organic Chemical Manufacturing Company, which put out a line of "Formosal" compounds. One was A-F-Sal (also sold under the name Urasol), claimed to be "Acetyl-Methylene-Disalicylic-Acid." This substance is alleged to be the basis of Befsal. In an investigation on the value of internal antiseptics, made for the Council on Pharmacy and Chemistry, Sollmann reported (in 1908) that he found A-F-Sal pronouncedly and persistently nauseating. While the A-F-Sal advertisements claimed that formaldehyde was gradually split off and acted as a urinary solvent, Sollmann found no evidence that formaldehyde was split off in the body, or that the compounds had any discoverable antiseptic action on the urine. He could find no ground for the claimed superiority over salicylates, and held the claim that "they are the most valuable salicylic acid compounds known" a gross exaggeration.

The manufacturer and a firm of chemists, Samuel Sadtler and Son, attacked the report. The Council appointed a referee, and after the examination of evidence, supplemented by independent work, the findings of Sollmann were confirmed. Subsequently the firm filed suit against the American Medical Association; but as in many other cases the suit never came to trial, and the vast amount of evidence in the possession of the Association was never utilized.

In circular letters sent out in 1924 by both Summers and Richard occurs the following paragraph:

> "The established proof of a-f-sal (acetyl-methylene-disalicylic acid) exerting the function of a scavenger in removing effete products from the system, was exhibited by Prof. Samuel P. Sadtler, Ph.D., LL.D., in pamphlets issued by *Journal of A. M. A.* in his evidence of the large percentage of salicyl-uric acid found in the urine, as a result of the combining power of the salicyl radical, when liberated from a-f-sal in the system, with a purin body."

The misleading character of this statement, which is identical with that used in advertising A-F-Sal twelve years ago, lies in the fact that the work of Sadtler referred to as "in pamphlet issued" by THE JOURNAL is the very evidence which was advanced by the firm and so effectively disposed of by the Council on Pharmacy and Chemistry whose report of the matter was published in reprint form!

### THE SPECIMENS

A package of Befsal was ordered from C. A. Harold, the Philadelphia pharmacist recommended by Dr. Lambert Ott. In due time a package arrived (price $3) containing two ounces of a black powder, having an odor resembling certain types of fertilizer. On the label appeared the following:

BEFSAL
Dibenzyl Diethyl-Methylene-disalicyl
—Dicinchoninic acid

Adult dose — 90 to 180 grains per day

DR. S. LEWIS SUMMERS
Producer of
Synthetic Organic Chemical Compounds
Fort Washington, Penna.

The A. M. A. Chemical Laboratory made some tests on the product and reported that it could not be considered a "synthetic" but appeared to be a crude mixture. The ash alone amounted to 12 per cent and consisted essentially of iron oxide. Elementary sulphur was present in the original material in relatively large amounts. The amount of material that was insoluble in boiling alcohol was 47 per cent; with cold alcohol (22 C.) the amount of insoluble material was 70 per cent. Tests indicated the presence of some combined salicylic acid. The presence of cinchoninic or phenylcinchoninic acid could not be confirmed. The product cannot, therefore, be considered a chemical compound with a definite formula as described by S. Lewis Summers; obviously it does not have the composition claimed for it.

Another specimen of Befsal was ordered, this time from the Synthetic Organic Products Co., New York. This bore a somewhat different label than on the specimen just described; thus:

BEFSAL
$C_{55}H_{42}O_{10}N_2$
Synthetic Organic
Products Co., Inc.
227 Sixth Ave. New York

The product itself also differed. It was a brown powder, with an aromatic odor resembling ethyl salicylate. Practically no ash was left after ignition. Like the other specimen, however, the product was a mixture of substances, one fraction of which was soluble in ether, another fraction soluble in alcohol. There was a considerable amount of resinous material present. Under the microscope the product appeared as a heterogeneous mixture and not as a definite compound. Combined salicylic acid was found to be present.

The Chemical Laboratory reports that while the product is not as crude as the specimen obtained from C. A.

Harold, yet it is obviously not a definite synthetic, and that it is highly improbable that it has such a formula as that ascribed to it ($C_{55}H_{42}O_{10}N_2$). The Laboratory concluded that the product known as Befsal is of varying and unreliable composition and that it is unlikely that such a substance as dibenzyldiethylmethylenedisalicylicdicinchoninic acid can exist.

### THE ADVERTISING

As mentioned before, Befsal is puffed by Dr. Lambert Ott. Circulars from both "S. L. Summers Producer of Organic Chemicals" or the "Synthetic Organic Products Company, Inc.," refer to an article by Dr. Ott, published in the August, 1922, issue of *American Physician.* Reprints of this article have been sent to physicians, many of whom have sent skeptical inquiries to THE JOURNAL concerning the product. Dr. Ott's article contains no scientific data, and reports very few cases, and no controls. Curiously enough, however, the conclusion of the article endorsing Befsal is almost word for word the same as that of an article praising A-F-Sal, published in 1911!

In common with the exploitation of "patent medicines" for rheumatism, there is dragged in the uric acid hypothesis—a hypothesis long ago discarded by scientific medicine. Dr. Summers, one of the promoter-producers, also endows Befsal with unusual virtues, claiming that the product possesses "marked internal antiseptic value and in sufficient dosage is more of a specific in acute rheumatism than is quinine in malaria. In fact, so potent in rheumatic disorders is Befsal that it can be used as a means of diagnosis."

## RAZ-MAH

### Another Nostrum for Asthma and Hay-Fever

*(Abstracted, with additions, from The Journal A. M. A., Feb. 28, 1925, p. 694)*

Are you kept awake by asthmatic attacks or hay-fever? "To sleep tonight, use Raz-Mah today." This is the slogan for a nostrum put out by Templetons, Inc., of Detroit, for sale in the United States, and by Templeton's Ltd., Toronto, for sale in Canada. The alleged history of the origin of this nostrum seems to vary, depending on whether one purchases the product as sold in Canada or that sold in the United States. The story given in the advertising circular that goes with the product sold in this country is to the effect that the writer of the circular had for ten years suffered with "hay fever or summer asthma." He tried innumerable treatments and got no relief, until finally "a chemist friend" suggested that he try a mixture which was later put on the market as Raz-Mah, and it brought him complete freedom from his trouble.

The Canadian circular is to the effect that Mr. J. G. Templeton, after "perfecting the formula for his rheumatic remedy," devoted his time to a specific for asthma, then:

> "By slow and careful study and experiment over several years a formula was finally arrived at which produced the most remarkable results. No case was too far gone, no attack too severe to respond to the treatment. Three years of actual test of this formula have convinced Mr. Templeton that he has evolved the ideal treatment for asthma and hay fever. Under the trade name of Raz-Mah this remedy is now offered to the public."

Inquiries were received from various parts of the United States and Canada asking for information regarding the composition of Raz-Mah, which, from the reports, evidently contained drugs of some potency. Dr. H. E. Young of Victoria, B. C., the Provincial Officer of Health for British Columbia, reported to The Journal more than four years ago that an analysis made by the National Department of Health at Ottawa of Raz-Mah as sold in Canada showed that each Raz-Mah capsule contained a little more than 4 grains of acetylsalicylic acid (aspirin), about ½ grain of caffeine and $^{7}/_{10}$ of a grain of bone-black. About the same time the A. M. A. Chemical Laboratory made some cursory tests of this preparation, and it also reported finding acetylsalicylic acid (aspirin), caffeine and charcoal.

In September, 1924, it was decided to make a more complete analysis of the preparation.

One original box of Raz-Mah manufactured by Templetons, Inc., Detroit, Michigan, was submitted to the A. M. A. Chemical Laboratory for examination. The box contained thirty-two capsules each containing an average of 0.42 gram (6.5 grains) of a crudely mixed grayish powder. Microscopic examination showed starch grains, some of which were colored by presence of iodine; crystals resembling acetylsalicylic acid (aspirin) were also present. Qualitative tests indicated the presence of caffeine, acetylsalicylic acid, iodide, carbon (charcoal[1]) calcium, magnesium, iron, sodium, potassium, sulphate and starch. There was also some other material which was either plant extract or material extracted from a charred substance (such as charcoal); this material was not identified. Arsenic compounds, emodin-bearing drugs, alkaloids other than caffeine or other antipyrectics than acetylsalicylic acid were not found. The amount of ash was 4.46 per cent. Quantitative determinations yielded the following:

---

[1] The presence of charcoal and impurities suggests that the caffeine might possibly have been added in the form of coffee roaster flue dust.

| | |
|---|---|
| Caffeine | 9.15 per cent. |
| Acetylsalicylic acid (aspirin) | 67.83 per cent. |
| Carbon (charcoal) | 10.75 per cent. |
| Iodide ($I^-$) | 2.26 per cent. |
| Moisture | 0.67 per cent. |
| Starch | 1.52 per cent. |
| Calcium ($Ca^{++}$) | 0.09 per cent. |
| Magnesium ($Mg^{++}$) | 0.18 per cent. |
| Sodium ($Na^+$) | 1.21 per cent. |
| Potassium ($K^+$) | 0.46 per cent. |
| Insoluble materials (other than charcoal) | 0.44 per cent. |
| Undetermined | 5.44 per cent. |
| | 100.00 per cent. |

From this analysis it appears that Raz-Mah is essentially a mixture of caffeine, acetylsalicylic acid and an iodide.

Another sample of Raz Mah (the contents of which were not submitted to quantitative examination) differed from the specimen analyzed in that oil of spearmint was present and iodide was absent. The market specimens, therefore, differ in composition.

Each capsule of Raz-Mah may be stated to contain approximately:

| | |
|---|---|
| Acetylsalicylic acid (aspirin) | 4½ grains |
| Charcoal | 1 grain |
| Caffeine | ½ grain |

The directions call for two capsules of Raz-Mah at a dose with from three to four doses a day. This means that the maximum daily dose (eight capsules) contains approximately 35 grains of acetylsalicylic acid (aspirin) and 4½ grains of caffeine. The presence of iodides in certain samples seems to be accidental, the Canadian chemists having, apparently, found none, and the A. M. A. chemists being unable to find any in some of the specimens examined. The variable composition may be due to the careless methods employed by nostrum manufacturers or it may indicate that, for reasons best known to themselves, the exploiters of Raz-Mah have seen fit to change the formula for their product.

As THE JOURNAL stated:

"It appears, then, that Raz-Mah, whose 'formula' was finally arrived at 'by slow and careful study and experimentation over several years,' is to all intents and purposes nothing more than powdered aspirin and caffeine. No wonder the 'patent medicine' interests fight to the last ditch against formula disclosure."

### Details of Analysis

*Caffeine.*—Caffeine was determined by two methods.

Accurately weighed samples were extracted with chloroform for four hours using the Soxhlet extractor. The chloroform was evaporated to a small bulk, transferred to a beaker and then 5 cc. of sodium hydroxide solution diluted with 20 cc. of water was added. (The sodium hydroxide solution retained the acetylsalicylic acid.) After shaking, the chloroform was drawn off and then the water layer was extracted twice more with chloroform using 30 cc. and 25 cc. of the solvent in the shake outs. It was necessary to centrifuge the combined chloroform extract to break down the emulsion that was present. The chloroform extract was evaporated to dryness. All of the resulting solid did not appear to be caffeine. Water was added and the insoluble portion was filtered off and discarded. The solution was made alkaline with a few drops of sodium carbonate solution. It was then extracted twice with chloroform. The chloroform was evaporated spontaneously and the residue weighed. A sample of the original specimen weighing 0.2083 gram yielded 0.0197 gram of caffeine. This is equivalent to 9.45 per cent. A second sample weighing 0.1723 gram yielded 0.0156 gram of caffeine. This is equivalent to 9.05 per cent. Both samples melted at 231 C.

In the second method a weighed sample was treated with 5 cc. of sodium hydroxide solution diluted with 50 cc. of water. The solution was filtered and extracted four times with chloroform using 30 cc., 25 cc., 20 cc., and 20 cc. respectively in the shake-outs. The chloroform extract was dried spontaneously and weighed. A sample weighing 0.4230 gram yielded 0.0374 gram of caffeine melting at 233.5 C. This amounts to 8.84 per cent. A second sample weighing 0.5514 gram yielded 0.0510 gram of caffeine. This is equivalent to 9.25 per cent.

*Acetylsalicylic Acid.*—The alkaline solution from which the caffeine was extracted in the second method of analysis for caffeine was made acid with diluted hydrochloric acid. It was then extracted four times with ether using 30 cc., 25 cc., 20 cc., and 20 cc. portions of the solvent. The ether was allowed to evaporate. The solid was then taken up with absolute ether several times to rid it of a slight odor of hydrochloric acid. The solid was finally weighed. The sample of the original specimen weighing 0.4230 gram yielded 0.2209 gram of salicylic acid melting at 155 C. This is equivalent to 68.10 per cent of acetylsalicylic acid. The sample weighing 0.5514 gram yielded 0.2857 gram of salicylic acid melting at 155 C. This is equivalent to 67.57 per cent acetylsalicylic acid.

*Iodide.*—A weighed sample of the original specimen was extracted to constant weight with chloroform. The undissolved material was percolated with 200 cc. of water, the temperature of which was 21 C. The filtrate was made up to 250 cc. A 100 cc. portion of this solution was acidified with nitric acid and the iodide precipitated with silver nitrate solution in the usual way. The precipitate was filtered, washed, dried, and weighed. A sample weighing 0.2803 gram yielded 0.0047 gram of silver iodide. This represents 2.21 per cent iodide. A second sample weighing 0.3506 gram yielded 0.0060 gram of silver iodide. This represents 2.31 per cent.

*Moisture.*—A sample of the original specimen weighing 0.5323 gram lost 0.0036 gram after standing in a vacuum over sulphuric acid for forty-eight hours. This is equivalent to 0.67 per cent.

*Starch.*—The sample after extraction with chloroform and cold water was percolated with 200 cc. of boiling water. The loss in weight was assumed to be due to starch. A sample weighing 0.2803 gram lost 0.0041 gram. This is equivalent to 1.46 per cent starch. Another sample weighing 0.3506 gram lost 0.0056 gram. This is equivalent to 1.59 per cent.

*Carbon.*—A sample of the original specimen was extracted with chloroform, cold water, hot water, strong hydrochloric acid, and sodium hydroxide solution. The residue was carefully washed with water, dried and weighed. It was then heated over the full flame of the Meeker burner. The loss in weight was assigned to carbon. A sample weighing 0.2803 gram lost 0.0304 gram. This is equivalent to 10.84 per cent. A sample weighing 0.3506 gram lost 0.0374 gram. This is equivalent to 10.66 per cent.

*Ash.*—A sample of the original specimen weighing 1.3561 grams was ashed in the usual manner. The ash amounted to 0.0605 gram. This is equivalent to 4.46 per cent.

*Acid Insoluble Ash.*—The ash was treated with diluted hydrochloric acid. The insoluble portion was filtered off and weighed. A sample of the original specimen weighing

1.3561 grams yielded 0.0060 gram of acid insoluble ash. This is equivalent to 0.44 per cent.

*Calcium.*—The acid filtrate from the insoluble ash was diluted to exactly 100 cc. A 50 cc. portion was diluted to 250 cc. and to the solution 3.5 grams of ammonium chloride and 1 gram of recrystallized oxalic acid were added. After heating the solution to boiling it was made alkaline with 1 per cent ammonia water. The solution stood twelve hours. The solid that separated was filtered, dried, and ignited to constant weight. Two 50 cc. aliquots gave 0.0008 and 0.0009 gram of calcium oxide. These weights are equivalent to 0.08 per cent and 0.09 per cent calcium respectively

*Magnesium.*—The filtrates from the calcium precipitates were evaporated to dryness and the ammonium salts expelled by gentle ignition. The residues were taken up in 70 cc. of warm diluted hydrochloric acid and filtered. The filtrates were treated with an excess of disodium hydrogen phosphate solution. The solutions were made alkaline with 10 per cent ammonia water and then 50 cc. of 10 per cent ammonia water was added in excess. After standing for several hours the precipitate was filtered, ignited and weighed as magnesium pyrophosphate. The weights were 0.0053 gram and 0.0058 gram. These weights are equivalent to 0.17 per cent and 0.19 per cent respectively.

*Sodium and Potassium.*—A sample of the original specimen weighing 0.7559 gram was ashed in the presence of a little sulphuric acid. The residue was taken up in diluted hydrochloric acid and the solution filtered. The filtrate was diluted to exactly 100 cc. A 25 cc. portion of this solution was made alkaline with ammonia water. Solutions of ammonium chloride, ammonium carbonate, and ammonium oxalate were added and the solid that separated after the solution had been standing a few hours was filtered off. The solution was made acid with sulphuric acid and then evaporated to dryness in the usual way. The weights of the combined sulphates in three determinations were 0.0092 gram, 0.0089 gram and 0.0091 gram. The average weight was 0.0091 gram.

Potassium was determined in the combined sulphates by the method described in Annual Reports of the A. M. A. Chemical Laboratory, Vol. 8, p. 54. Two determinations yielded 0.0016 and 0.0028 gram of platinum, respectively. The average weight was 0.0022 gram of platinum. These determinations are equivalent to 1.21 per cent sodium and 0.46 per cent potassium.

## RINEX

### A Mixture of Aspirin, Phenacetin and Quinine Sold as a Cure for "Colds," Hay-Fever and Asthma

*(Abstracted, with additions, from The Journal A. M. A., April 11, 1925, p. 1139)*

An increasing number of inquiries has come to THE JOURNAL asking for information regarding "Dr. Platt's Rinex Prescription" advertised and recommended for "Asthma, Catarrh, Hay Fever, Rose Fever, Bronchitis, and Other Throat Affections" and also for "Head Colds or Coryza." The product has been widely advertised in the newspapers, and samples have been freely distributed. The preparation is put out by the Clinical Laboratories Company of Cleveland, Ohio. No information is given regarding the composition of the preparation, but under the heading "What Rinex Is" this statement appears:

> "Rinex is a Physician's prescription, developed and perfected in the successful treatment of more than 7,000 clinical cases of Asthma, Hay Fever, Catarrh, Head Colds and other respiratory diseases. It is most carefully prepared from drugs of assured U. S. P. standard by one of the largest and most highly regarded Pharmaceutical Manufacturers."

Some of the claims made for Rinex in newspaper and other advertising are:

> "KILLS COLDS — QUICK! Guaranteed Relief in 5 Hours."
>
> "ROSE FEVER CURBED IN 24 HOURS. Every trace—fearfully runny eyes and nose—sneezing, headache, fever—vanishes in 24 hours with Cleveland specialist's new internal prescription."
>
> "ASTHMA SPECIALIST GUARANTEES RELIEF."
>
> "HAD COLDS CONQUERED IN 5 HOURS."

Every "patent medicine" has its own story of origin. Rinex is no exception. Here is the brief story of the alleged genesis of "Dr. Platt's Rinex Prescription":

> "Dr. M. G. Platt, of the Clinical Laboratories, Cleveland, after 8 years' intensive study of hay fever, asthma, catarrh and kindred affections—has recently perfected a new and amazingly successful method of treatment, entirely different from any heretofore used. With characteristic professional caution, the doctor does not call the new treatment a cure. But with it he has been able to banish all symptoms in 24 hours—not in a few isolated instances, but actually in 95 per cent. of the thousands of cases which have come under his clinical observation."

In order that the public and the medical profession might know just what was in this "Safe Scientific treatment for the Relief of All Forms of Asthma, Catarrh and Hay Fever" and just what drugs in it "instantly attack the toxic poisons" [*Sic!*], several packages of the nostrum were purchased.

A number of original packages of Dr. Platt's Rinex Prescription (Clinical Laboratories Co., Cleveland) were submitted to the A. M. A. Chemical Laboratory for examination. Each package contained thirty capsules and fifteen yellowish-white tablets.

*Capsules.*—These contained a brown, heterogeneous powder having an odor resembling camphor; the average weight of the contents of each capsule was 0.35 Gm. (5.4 grains). On the bottle label (in very small type) the presence of 1 per cent of acetphenetidin is declared. Tests indicated the presence of acetphenetidin, acetylsalicylic acid, quinine, camphor, extractives from emodin-bearing drugs, tragacanth, calcium, magnesium, carbonate, sulphate, acid-insoluble substance (talc) and traces of sodium, potassium and phosphate. Tests for the following substances were negative: antipyrine, acetanilid, amidopyrine, belladonna alkaloids, caffeine, arsenic, aconitine, strychnine, bromide, iodide, hexamethylenamine, sucrose and lactose.

Two lots of capsules were examined; on one lot (Lot A) determinations of solubility fractions were made. On the other lot, the following quantitative estimations were made:[1]

| | |
|---|---|
| Loss in vacuum over sulphuric acid (moisture) | 1.61 per cent. |
| Ash | 12.17 per cent. |
| Acid-insoluble material (talc) | 4.11 per cent. |
| Quinine | 3.02 per cent. |
| Acetphenetidin | 16.2 per cent. |
| Acetylsalicylic acid | 34.8 per cent. |

From the analytic results, it is concluded that each capsule contains as its essential ingredients approximately:

| | |
|---|---|
| Aspirin | 2 grs. |
| Phenacetin | 1 gr. |
| Quinine | 1/6 gr. |

The balance consists of an extractive from an emodin-bearing drug (such as debitterized cascara), a very small amount of camphor, inert material and excipients.

*Tablets.*—These were yellowish-white with an odor like oil of peppermint; the average weight of each tablet was 0.3 Gm. (4¾ grains). Tests for sulphates, chlorides, phosphates, emodin-bearing drugs, alkaloids and heavy metals were negative. Sodium, carbonate, sucrose (cane sugar), a trace of vegetable tissue, an acid-insoluble substance, probably talc, and traces of calcium and magnesium were present. Quantitative analysis gave the following results: sodium bicarbonate 72.82 per cent, sucrose 24.58 per cent, acid-insoluble 1.55 per cent, undetermined 1.08 per cent.

From the results of the analysis, the composition of Rinex tablets is essentially as follows:

| | |
|---|---|
| Baking soda | 73 per cent. |
| Sugar | 24.5 per cent. |
| Talc | 1.5 per cent. |
| Excipient | 1 per cent. |

Each tablet contains about 3 4/10 grains of baking soda and 1 1/10 grains of sugar.

In commenting, THE JOURNAL stated:

"Summed up then, it seems that Dr. Platt's Rinex Prescription is essentially a mixture of 2 grains of aspirin, 1 grain of acetphenetidin and 1/6 grain of quinine, with a small amount of laxative vegetable extractives and camphor. The supplementary treatment is nothing more striking than tablets of baking soda. Yet the public might well get the idea that Rinex is a combination of substances about which the medical profession is ignorant and that 'Dr. Platt' was renowned in his profession, although he is a man of whom the medical profession generally has never heard except possibly through the advertising of this 'patent medicine.' This is typical of nostrum exploitation. Well-known drugs used for years by the medical profession are put out under a fancy name, the public being kept in ignorance of the ingredients in order that the essential factors for successful 'patent medicine' exploitation—secrecy and mystery—may be maintained."

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[1] On Lot A, of which there was a large amount of material, determinations showed calcium ($Ca^{++}$) 1.2 per cent.; magnesium ($Mg.^{++}$) 0.66 per cent.; sulphate ($SO_4^{--}$) 2.7 per cent. and phosphate 0.15 per cent. This is equivalent to approximately 5 per cent. calcium sulphate (gypsum) and 3 per cent. magnesium carbonate, U. S. P.

## Details of Analysis

### CAPSULES

Some of the capsules were emptied as completely as convenient and the contents weighed. The contents of 90 capsules weighed 30.9256 Gm., equivalent to an average of 0.34 Gm. each, or about 5.3 grains each. The contents of another lot of 60 capsules weighed 20.9314 Gm., equivalent to 0.35 Gm., or about 5.4 grains each. Average for 150 capsules 5.4 grains each.

*Loss on Drying.*—A weighed portion of the material was dried at 100 C. to approximately constant weight. This was found to produce decomposition and the method was abandoned. The findings are given as a matter of record. The loss from 2.0591 Gm. of material was 0.3045 Gm., equivalent to 14.78 per cent; a duplicate which weighed 3.0124 Gm. lost 0.4458 Gm., equivalent to 14.8 per cent. Average, 14.8 per cent of loss on drying. The method finally adopted was to dry a weighed portion over sulphuric acid in a vacuum. A weight of 1.0090 Gm. lost 0.0163 Gm., equivalent to 1.62 per cent. A duplicate of 1.0960 Gm. lost 0.0175 Gm., equivalent to 1.61 per cent. Average, 1.61 per cent.

*Ash.*—A weighed quantity of the material was heated to low redness, the residue cooled and moistened with water. The residue was dried at 120 C. and again heated until the weight became constant. The ash from 1.0269 Gm. of material weighed 0.1260 Gm., equivalent to 12.27 per cent. A duplicate of 1.0277 Gm. of material gave 0.1251 Gm. of ash, or 12.17 per cent.

*Acid-Insoluble Ash.*—The ash was treated with diluted hydrochloric acid for several hours and the insoluble portion collected in a tared Gooch crucible, washed, dried, heated, and weighed. From 1.0269 Gm. of original material 0.0427 Gm. of acid-insoluble ash was obtained, or 4.15 per cent. A duplicate of 1.0277 Gm. of material gave 0.0419 Gm. of acid-insoluble ash, or 4.07 per cent. Average, 4.11 per cent.

*Calcium.*—Calcium was determined as follows:

The filtrate containing the acid-insoluble ash (from the determinations of acid-insoluble ash) was evaporated to dryness on the water-bath, 10 cc. of water added and the mixture again evaporated to dryness. The residue was taken up in water, 0.5 Gm. of citric acid added, the mixture warmed and filtered to remove traces of insoluble material. Ammonium oxalate solution was added to the filtrate, the mixture kept at a temperature of about 90 C. for 2 hours and the precipitated calcium oxalate collected, dried, heated, and the residue weighed as calcium carbonate in the usual way.

The calcium carbonate from 3.0124 Gm. of material weighed 0.091 Gm., equivalent to 1.21 per cent of calcium. A duplicate of 2.0591 Gm. of material gave 0.0608 Gm. of calcium carbonate, equivalent to 1.18 per cent of calcium. Average 1.20 per cent of calcium sulphate ($CaSO_4.2H_2O$). This is equivalent to 5.16 per cent of calcium.

*Magnesium.*—The filtrate from the calcium determinations was evaporated to dryness, the residue heated to remove citric acid and ammonium salts and this residue digested with diluted hydrochloric acid for several hours to convert any pyrophosphates into normal phosphates. The solution was filtered to remove traces of insoluble matter, a few cc. of sodium phosphate solution added and the solution made alkaline with ammonia water After standing twenty-four hours the precipitate was collected in a tared Gooch crucible, dried and ignited to magnesium pyrophosphate.

From 3.0124 Gm. of material, 0.0939 Gm. of magnesium pyrophosphate was obtained, equivalent to 0.68 per cent of magnesium. A duplicate of 2.0591 Gm. of original material yielded 0.0608 Gm. of magnesium pyrophosphate, equivalent to 0.65 per cent of magnesium. Average, 0.66 per cent of magnesium. This is equivalent to about 2.66 per cent of magnesium carbonate U. S. P.

*Acetphenetidin and Acetylsalicylic Acid.* A quantity of the material was placed in a weighed Gooch crucible and the crucible and contents weighed to obtain the weight of material taken. A quantity of dry asbestos was added to hold the material in place. The upper layer of asbestos was then weighted down by placing a perforated Gooch crucible bottom on it and the whole again weighed. The material was extracted in a Soxhlet apparatus with a mixture of 90 volumes of chloroform and 10 volumes of ether until extraction was complete. Completion of the extraction was determined by removing the crucible from the apparatus from time to time, drying it at 100 C. and weighing. The solvent was then shaken repeatedly in a separator with 1 per cent hydrochloric acid until the alkaloid had been completely removed. The solvent was then filtered through dry filter paper into a 250 cc. volumetric flask and the volume made up to the mark with chloroform. Aliquot portions of the solution were then evaporated in weighed dishes on a steam radiator by the aid of a fan, and the residue dried first over sulphuric acid and afterward over soda lime. The residue from 100 cc. of solvent, equivalent to 1.2618 Gm. of original material, weighed 0.6619 Gm., or 52.45 per cent. A duplicate from 50 cc. of solvent, equivalent to 0.6309 Gm. of original material, weighed 0.3279 Gm., or 51.97 per cent. The residue from 100 cc. of solvent, representing 0.8338 Gm. of material, weighed 0.4248 Gm., or 50.94 per cent. The residue from a duplicate of 50 cc., representing 0.41692 Gm. of original material, weighed 0.2116 Gm., equivalent to 50.75 per cent. Average, 51.53 per cent of chloroform-ether soluble material after removal of the alkaloid.

Still another method was employed for extracting the powder from the contents of the capsules. This one, which was believed to be less subject to errors than the one previously described in this report, is as follows:

> A weighed portion of the material was placed in a Gooch crucible, percolated in the cold with the chloroform-ether mixture (9–1) until no further material was removed by the solvent. The residue was then extracted in a Soxhlet apparatus with more of the solvent to exhaustion. The two extracts were then evaporated in the cold by the aid of a fan, and the residues dried over sulphuric acid in a vacuum. The values obtained were added. These residues contain the quinine, originally present in the material, or at least the most of it.

The extractives from 3.0248 Gm. of the material weighed 1.6549 Gm. by cold percolation, equivalent to 54.71 per cent. By hot extraction in a Soxhlet apparatus the residue in the thimble gave a weight of 0.0678 Gm. additional, or 2.24 per cent. Total 56.95 per cent. A weight of 1.2044 Gm. of material gave 0.6585 Gm. of residue by cold percolation, equivalent to 54.67 per cent. The residue in the thimble gave a weight of 0.0188 Gm. additional, equivalent to 1.56 per cent. Total extract, 56.23 per cent. Average, 56.59 per cent total extract.

Two methods for separating the acetylsalicylic acid from the acetphenetidin were carried out from this point. One was an adaptation of the Emery-Spencer-LeFebre method for separating acetphenetidin from salol (*Jour. Ind. Eng. Chem.* 7, 681, 1915) by alkaline treatment. In this method 10 cc. of 2.5 per cent sodium hydroxide solution were added to the residue obtained by chloroform-ether extraction and subsequent evaporation of the solvent, and the mixture heated on the steam bath for 5 minutes. The mixture was cooled at once, transferring to a separator using 10 cc. of water and 25 cc. of chloroform for washing. The solution was shaken thrice with 25, 15 and 10 cc. of chloroform respectively, the bulked solvent washed with 25 cc. of water, the solvent evaporated by means of a fan and gentle heat, the residue dried at 100 C. for 10 minutes, cooled and weighed as acetphenetidin.

The acetphenetidin produced from the residue obtained from 3.0248 Gm. of original material weighed 0.4946 Gm., equivalent to 16.35 per cent. The acetphenetidin produced from the residue obtained from 1.2044 Gm. of original material weighed 0.1938 Gm., equivalent to 16.09 per cent. Average, 16.22 per cent.

The second method for acetphenetidin used was that of Emery *et al.* (Ibid.) by acid hydrolysis and regeneration of the acetphenetidin by acetic anhydride after removal of the salicylic acid and emodin extractives by chloroform from acid solution. The method used is as follows:

> Add 10 cc. of dilute sulphuric acid to the chloroform-ether soluble residue and digest on the steam-bath, heat until the liquid has been reduced one half. Add 10 cc. of water, continue the digestion as before, add a second 10 cc. of water and evaporate the solution to 5 cc. Transfer the residual liquid by pouring and washing with about 20 cc. of water to a small separator and extract successively with 15, 10 and 5 cc. of chloroform, washing each portion as obtained with 5 cc. of water in a second separator, in order to recover traces of phenetidin sulphate, possibly taken up by the chloroform. Reserve the washings and reject the chloroform. To the aqueous acid solution of phenetidin sulphate in the first separator into which also the wash water from the second separator has been drawn, add sodium bicarbonate in small portions until an excess of this reagent persists at the bottom of the separator after complete neutralization of the sulphuric acid. Add 25 cc. of chloroform and for every 100 mg. of acetphenetidin known or believed to

> be present 5 drops of acetic anhydride, shake for some time vigorously, pass the nearly clarified solvent into a second separator containing 5 cc. of water, shake and filter the solvent through a small dry filter into a 200 cc. Erlenmeyer flask. Repeat the shaking process with chloroform twice, washing and filtering each time as before. Collect the solvent in the Erlenmeyer flask. Distil to small volume and transfer the chloroformic residue to a tared 50 cc. beaker using a little fresh chloroform for rinsing. Evaporate on a steam bath to apparent dryness, finally removing any pronounced excess of acetic anhydride by repeated additions of 1 cc. portions of fresh chloroform (to which a drop of alcohol has been added) and subsequent evaporation. Allow the nearly colorless, crystalline residue of acetphenetidin to stand some time in the open, or better in a vacuum desiccator over lime, in order to eliminate the last traces of acetic anhydride. Weigh at intervals until constant.

The acetphenetidin regenerated from 2.1005 Gm. weighed 0.3607 Gm., equivalent to 17.17 per cent. Since this result checked reasonably well with the results from the alkaline hydrolysis method and with the declaration on the label, a duplicate was not carried out.

Acetphenetidin was identified by the tests given below, each of which gave a positive reaction:

> A drop of acetic acid and 0.5 cc. of tenth-normal iodine were added to 1 to 2 Mg. of the separated material contained in a test tube. The mixture was warmed to about 40 C., and a drop of hydrochloric acid added. Reddish-brown needles separated in a few minutes. It is stated that if acetphenetidin alone be present, its periodid separates almost immediately in the form of reddish-brown leaflets or needle-like crystals. This test which was worked out by Dr. Emery, is said to be so delicate that as little as 0.5 Gm. of acetphenetidin may, if alone, be detected in the form of its characteristic periodid.
>
> A portion of the separated material was boiled with a few cc. of diluted nitric acid. An intense orange-yellow color resulted.
>
> A portion of the separated material was boiled with a few cc. of diluted sulphuric acid, the mixture diluted with water, the resultant mixture cooled and filtered. A drop of potassium dichromate added to the filtrate gave a ruby-red color.

Attempts were made to determine the acetylsalicylic acid by direct titration of the residue obtained by the chloroform-ether extraction (after removal of the alkaloid) with half-normal alcoholic potassium hydroxide or with tenth-normal potassium hydroxide, using phenolphthalein as indicator. For some reason remaining unexplained the end joint was was not starch, the results were low, and the method had to be abandoned. It is possible that the presence of emodin-bearing extractives vitiates the determination of the end point.

To check the accuracy of the titration method on pure acetylsalicylic acid a known weight of acetylsalicylic acid was mixed with an equal weight of acetphenetidin, the mixture dissolved in neutral alcohol and the solution titrated with half-normal alcoholic potassium hydroxide, using phenolphthalein as indicator. A weight of 0.5627 Gm. of acetylsalicylic acid and 0.5 Gm. of acetphenetidin required 6.45 cc. of potassium hydroxide, equivalent to 6.2 cc. of half normal potassium hydroxide. This is equivalent to 0.5582 Gm. of acetylsalicylic acid, or 99.2 per cent.

That the results on the unknown were not correct is shown by the fact that on saponifying the titrated residues with an excess of potassium hydroxide, subsequent acidification with hydrochloric acid, shaking with ether and evaporation of the solvent a quantity of salicylic acid was obtained in excess of that expected from the amount of acetylsalicylic acid indicated by the titration. The results obtained are given as a matter of record. The acetylsalicylic acid in 0.5665 Gm. of chloroform-ether extract (representing 1.1282 Gm. of original material) required 3.127 cc. of half-normal alcoholic potassium hydroxide, equivalent to 0.2815 Gm. of acetylsalicylic acid, or 24.94 per cent. One-fourth of a duplicate residue weighing 1.2923 Gm., representing 2.7932 Gm. of original material, required 1.95 cc. of half-normal potassium hydroxide (factor 0.961), equivalent to 24.23 per cent acetylsalicylic acid. A duplicate of this aliquot required the same amount of half-normal alcoholic potassium hydroxide. Average, 24.47 per cent of acetylsalicylic acid. A residue from another lot of material weighing 0.2116 Gm., representing 0.41692 Gm. of original material, required 5.935 cc. of tenth-normal sodium hydroxide, equivalent to 25.63 per cent of acetylsalicylic acid. A duplicate weighing 0.3279 Gm., representing 0.63092 Gm. of original material, required 9.55 cc. of tenth-normal sodium hydroxide, equivalent to 27.25 per cent of acetylsalicylic acid. Average, 26.44 per cent of acetylsalicylic acid.

It is probable that in the extraction of the acetylsalicylic acid by solvents in the Soxhlet apparatus some of the acetylsalicylic acid in the mixture is hydrolyzed with subsequent loss of acetic acid when the chloroformic solution is evaporated.

An odor of acetic acid was noted during the evaporation of some of these solutions. In order to check on this the amount of free salicylic acid produced by saponification of the acetylsalicylic acid was estimated. This was carried out by acidifying the alkaline solution from which the acetphenetidin had been removed, shaking the solution with chloroform-ether mixture (2-1 by volume), evaporation of the solvent, drying the residue over sulphuric acid in a vacuum and weighing as salicylic acid. The salicylic acid obtained by this method was contaminated with small amounts of anthraquinones. The salicylic acid from 3.0248 Gm. of original material weighed 0.8025 Gm., equivalent to 26.54 per cent of salicylic acid or to 34.71 per cent of acetylsalicylic acid. A duplicate of 1.2044 Gm. gave 0.3214 Gm. of salicylic acid, equivalent to 26.68 per cent of salicylic acid or to 34.79 per cent of acetylsalicylic acid. Average, 34.75 per cent of acetylsalicylic acid.

*Emodin-Bearing Extractives.*—The presence of emodin-bearing extractives was indicated by applying the Borntraeger test to a portion of the chloroform-ether extractive from the contents of the capsules. The presence of such extractives was made evident all through the analysis by the red color of the alkaline solutions and the yellow color of the acid solutions. No attempt was made to assay the preparation for anthraquinone derivatives as the quantity was believed to be comparatively small.

*Quinine.*—Quinine was determined by repeatedly shaking out the chloroform-ether extract obtained in the Soxhlet extraction with dilute hydrochloric acid. The acid layers were united and the solution washed once with 10 cc. of chloroform, the solvent being added to the original extract. The bulked aqueous, acid solution was made alkaline with ammonia water and the solution shaken with 25, 15 and 10 cc. of chloroform respectively, the portions of solvents united, the solution washed once with water and evaporated by means of a fan and gentle heat. The residue was dried at 100 C. for 10 minutes and weighed. The total alkaloids from 3.0248 Gm. of material weighed 0.0915 Gm., equivalent to 3.02 per cent. A duplicate of 1.2644 Gm. of material gave 0.0362 Gm. of alkaloid, equivalent to 3.01 per cent. Average, 3.02 per cent of total alkaloid.

The alkaloid was not alkaline to phenolphthalein (atropine) and did not give the tongue test for aconitin nor the fading purple test for strychnine.

The alkaloid was dissolved in about 5 cc. of diluted hydrochloric acid, the solution evaporated to dryness and the residue taken up in 10 cc. of water.

Quinine was identified in the solution by the following tests:

> Add a few drops of bromine water to a solution of about 0.01 Gm. of quinine hydrochloride in 1 cc. of water and add 1 cc. of ammonia water. An emerald-green color is produced.
>
> Add a few drops of ammonium oxalate solution to a solution of about 0.010 Gm. of quinine hydrochloride in 1 cc. of water. A white, crystalline precipitate results.
>
> Add a few drops of sodium salicylate solution (10 per cent) to a solution of about 0.01 Gm. of quinine hydrochloride in 1 cc. of water. A voluminous, white, crystalline precipitate results.
>
> Add a few drops of potassium sodium tartrate solution (10 per cent) to a solution of 0.01 Gm. of quinine hydrochlorid in 1 cc. of water. A white, crystalline precipitate results.

*Caffeine.*—The absence of caffeine was demonstrated by the following test:

> A specimen of the acetphenetidin which was recovered from the material by the alkaline hydrolysis method was treated on the water bath with 10 cc. of diluted sulphuric acid until the volume had been reduced to about 5 cc. Ten cc. of water were then added and the solution again evaporated to 5 cc. Ten cc. of water again were added and the volume reduced to 5 cc. by evaporation. The cooled acid solution was filtered and the filtrate shaken with chloroform. The residue remaining on evaporation of the solvent was negligible. This did not give the murexide test for caffeine.
>
> A portion of the quinine, obtained as described in another portion of this report, was dissolved in diluted sulphuric acid, the acid solution repeatedly shaken with chloroform and the solvent evaporated to dryness. The residue was negligible. This did not give the murexide test for caffeine.

*Alcohol-Soluble (After Chloroform-Ether Extractions).*—After the extraction by chloroform-ether had been completed, the material remaining in the Soxhlet apparatus was extracted with alcohol and the remaining residue later extracted with water, the crucible and contents in the extraction by each solvent being removed from the apparatus from time to time, dried and weighed. The losses in weight were compared with the residues obtained by evaporating the solution of the material extracted (or aliquots). A weight of 3.1546 Gm. lost 2.0423 Gm. to chloroform-ether, equivalent to 64.74

per cent. A duplicate of 2.0846 Gm. lost 1.3372 Gm., equivalent to 64.15 per cent. A third sample weighing 3.6910 Gm. lost 2.3430 Gm., equivalent to 63.47 per cent. Average, 64.12 per cent loss to chloroform-ether. A weight of 3.0248 Gm. of material from another lot of the preparation lost 1.9568 Gm., equivalent to 64.72 per cent. A duplicate of 1.2044 Gm. of material lost 0.7491 Gm., or 62.20 per cent. Average of the last two determinations, 63.46 per cent. The losses to alcohol of these five samples were respectively 0.2602 Gm., 0.1659 Gm., 0.3287 Gm., 0.2450 Gm., and 0.1095 Gm., equivalent to 8.25, 7.96, 8.79, 8.09 and 9.09 per cent respectively. Average, 8.43 per cent loss to alcohol. The losses found for the water extractions were respectively, (1) undetermined, (2) 0.1569 Gm., (3) 0.2727 Gm., (4) 0.3562 Gm., and (5) 0.1471 Gm. These results are equivalent to (2) 7.52 per cent., (3) 7.39 per cent., (4) 11.77 per cent., and (5) 12.21 per cent. Average, 9.72 per cent loss to water.

*Sulphate.*—The residue obtained on drying some of the material was repeatedly digested with dilute hydrochloric acid, filtering between each digestion. The filtrate was heated to boiling and an excess of barium chloride solution added. The precipitate was collected, heated and weighed under the usual precautions. The barium sulphate from 2.0134 Gm. of material weighed 0.1331 Gm., equivalent to 2.72 per cent of sulphate ion ($SO_4^{=}$). A duplicate of 2.0578 Gm. of material gave 0.1357 Gm. of barium sulphate, equivalent to 2.71 per cent of sulphate ion. Average, 2.72 per cent sulphate ion. This is equivalent to 4.87 per cent of hydrated calcium sulphate ($CaSO_4.2H_2O$).

## TABLETS

*Average Weight of Tablets.*—Fifteen of the tablets were weighed. The weight was 4.5495 Gm., equivalent to 0.3033 Gm. each. This is equivalent to about 4.7 grains each.

*Water Insoluble and Acid Insoluble.*—A weighed portion of the material was dissolved in cold water so far as possible and the insoluble material collected in a tared Gooch crucible, dried at 100 C. and weighed. The insoluble residue from 4.4329 Gm. of the material weighed 0.1187 Gm., equivalent to 2.68 per cent. A duplicate of 4.0035 Gm. gave the water insoluble residue of 0.1096 Gm., or 2.73 per cent. Average, 2.71 per cent of water insoluble material. The water insoluble residue was heated to low redness to destroy organic matter and the residue dried, heated and weighed. From 4.4329 Gm.

of material an acid insoluble residue of 0.0759 Gm. was obtained, equivalent to 1.77 per cent. In a duplicate, the water-insoluble residue was treated with acid and the insoluble residue dried and weighed before the organic matter was burned away. The acid insoluble residue from 4.0035 Gm. sample weighed 0.0781 Gm., or 1.95 per cent. The residue after ignition (acid-insoluble) weighed 0.0533 Gm., or 1.33 per cent. Average of acid-insoluble is 1.55 per cent. In this sample the loss by burning amounted to 0.0248 Gm., equivalent to 0.62 per cent excipient.

*Sodium Bicarbonate.*—The filtrate from the water-insoluble material was made up to 500 cc. with water and aliquots of 15 cc. each treated with a measured excess of tenth-normal sulphuric acid. The excess was titrated back with tenth-normal potassium hydroxide, using phenolphthalein as indicator and boiling repeatedly to insure removal of carbon dioxide. The sodium bicarbonate from 15 cc. of the diluted solution, representing 0.136485 Gm. of material, consumed 11.92 cc. of tenth-normal sulphuric acid, equivalent to 1.0015 Gm. of sodium bicarbonate, or 73.35 per cent. A duplicate of 15 cc. consumed 11.80 cc. of tenth-normal sulphuric acid, equivalent to 72.55 per cent. A third titration consumed the same quantity of acid as the second titration. Average, 72.82 per cent of sodium bicarbonate.

*Sucrose.*—The water-soluble filtrate was polarized with a 200 mm. tube at 20° C. using sodium light. The rotation values were 2.98° and 2.95°. Average, 2.965°, equivalent to 24.75 per cent of sucrose. After standing two weeks in the solution containing sodium bicarbonate the rotation was again observed and was found not to have changed appreciably.

## INCOMPATIBILITY OF MERCUROCHROME-220 SOLUBLE WITH QUININE AND UREA HYDROCHLORIDE AND ALKALOID SALTS

A query and its reply were published in THE JOURNAL, A. M. A., May 9, 1925, p. 1444, as follows:

> *To the Editor:*—What sort of chemical reaction, if any, would occur from the combining of equal parts of a 2 per cent. aqueous solution of mercurochrome-220 soluble and a 10 per cent solution of quinine and urea hydrochloride? I have made up a solution of these, and I fail to see any precipitation, but would like your idea of the usefulness of such a solution, or any other percentage of either of the ingredients mentioned.
>
> E. E. DARGATZ, M.D., Kinsley, Kan.

Answer.—The A. M. A. Chemical Laboratory reports that when a solution of mercurochrome-220 soluble, 2 per cent, is mixed with an equal volume of a solution of quinine and urea hydrochloride, 10 per cent, a precipitate results. This chemical incompatibility appears to be due to the interaction of the rather acid solution of quinine and urea hydrochloride (which was found to have $p_H$ less than 4) on the basic mercurochrome solution, whereby the sodium is split off and the relatively insoluble anhydride form of mercurochrome (di-brom-hydroxy-mercuri-fluorescein), together with some quinine, precipitates. Experiments made in the Laboratory, but which have not yet been reported, indicate that *fresh* solutions of mercurochrome-220 soluble contain such an exceedingly small concentration of mercuric ions that there is little likelihood of its acting as an alkaloidal precipitant by forming complex compounds of alkaloid and mercury containing substance. The general incompatibility of mercurochrome-220 soluble with many other alkaloidal salts has been reported by Warren (Incompatibility of Mercurochrome-220 Soluble with Local Anesthetics and Alkaloids, The Journal, April 14, 1923, p. 1091). In all cases alkaloidal salts of strong acids were used, so that the precipitate was probably a mixture of the free alkaloid and the di-brom-hydroxy-mercuri-fluorescein, though this was not brought out in the report. Warren reported no precipitate with coniine hydrochloride and mercurochrome-220 soluble; recent experiments with coniine hydrobromide, however, gave the characteristic precipitate.

It is inadvisable, therefore, to employ "solutions" of both alkaloids and mercurials whether or not the mercurial is in the form yielding mercuric ions (as potassium mercuric iodide), which precipitates complex alkaloid-mercuri compounds, or as a relatively nonionizable substance, which latter, if treated with an alkaloid salt, yields the insoluble form of the mercurial, together with the insoluble ("free") alkaloid.

## "MERCUROCHROME-220 SOLUBLE" INSOLUBLE IN ALCOHOL

A query and its reply were published in The Journal, A. M. A., May 9, 1925, p. 1445:

> *To the Editor:*—Please inform us as to the manner of making up an alcoholic solution of mercurochrome. We have found that mercurochrome is not directly soluble in absolute alcohol.
>
> Steptoe Valley Hospital, East Ely, Nev.

Answer.—Preliminary tests made in the A. M. A. Chemical Laboratory show that "mercurochrome-220 soluble" is much less soluble in alcohol than in water. In fact, the laboratory was not able to make an alcoholic solution stronger than 0.01 per cent mercurochrome, using 95 per cent alcohol. In making these experiments, both the sodium salt and the anhydride form were used. There appears to be little difference in the solubility of these two forms. There is a sufficient amount of "mercurochrome-220 soluble" in alcohol to color the alcohol, but it is highly improbable that the amount is sufficient to be of practical therapeutic importance.

## MIZAR

### Mr. Sorokowski's Red Pepper Cure for Rheumatism

*(Reprinted, in part, from The Journal A. M. A., July 18, 1925, p. 212)*

J. Sorokowski, who used to do business from 2424 West Superior Street, Chicago, but is now, apparently, operating from a west side suburb, Oak Park, sells (especially to the foreign element) a product that he calls "Mizar" as "the most effective remedy for rheumatism." Mizar comes in the form of an ointment, scented with bergamot and lemon. The instructions are to rub it on the parts affected and then bandage and keep the parts warm. Sorokowski states that on the second or third day an eruption will appear with itching. "Such eruption," says Sorokowski, "proves that the cause of ailment moves to the surface of the body—you will experience some swelling and redness, but don't get alarmed for that's the way Mizar is doing his work."

Some months ago a physician who does work in the dermatologic department of one of the free dispensaries in Chicago wrote in part as follows:

"About the middle of last winter a middle aged man came in with a severe dermatitis of one arm and leg. The patient had been using Mizar salve for rheumatism and wherever he had applied the salve, and only on these places, he had developed an acute severe dermatitis.

"Last Wednesday another Polish patient, an adult man, came into the clinic with the following history: A friend recommended 10 days before that he try Mizar salve for his rheumatism, which he did. The next day he stated that his legs became fiery red. He was obliged to go to the Cook County Hospital for a week. When seen in the clinic ten days after the one and only application of this salve he still had an acute dermatitis of both legs with some involvement of the scrotum and patchy areas on the hands and face.

"Briefly, here are two cases of dermatitis venenata from a salve called Mizar. Enclosed is the literature that accompanies a jar of this salve. The picture, name and address all appear on the jar. The salve is put up in a jar with a metal top (similar to commercial cold cream jar). It holds about two ounces or perhaps a little more. The retail price is $4.25 a jar, which is what each of the two patients paid."

More recently we received a letter from a physician in Detroit, accompanied by a jar of Mizar. This physician wrote in part as follows:

"Mizar is being sold here in Detroit among foreigners, for rheumatism, gastric ulcer, hernia and everything. The price charged is $4.25. I had a patient under my treatment with a peculiar rash from this salve—this prompted me to write to you."

A jar of Mizar was obtained, and the A. M. A. Chemical Laboratory made some tests in orded to determine the irritating substance responsible for the cases reported.

The following report was published in THE JOURNAL:

One original package of Mizar (Joseph Sorokowski, Chicago) was submitted to the Laboratory for examination. The jar contained about 2 ounces (60 Gm.) of a soft ointment having a pale, cream-yellow color and an odor suggestive of a mixture of bergamot and lemon oils. The taste was exceedingly pungent, thus suggesting the presence of capsicum extractives.

Qualitative tests indicated the absence of alkaloids, sodium borate (borax), and compounds of the heavy metals, such as lead, mercury, antimony, arsenic and bismuth; barium and calcium compounds were not found. Tests for volatile oil of mustard and for cantharides and ginger were negative. Soap, a saponifiable fat, petrolatum and considerable amounts of extractives from capsicum were present. Organoleptic tests indicated that the preparation contained capsicum extractives equivalent to about 1 Gm. of oleoresin of capsicum in 100 Gm. of material The amount of ash was 2.2 per cent. The total solids amounted to 77 per cent, about one half of which was petrolatum and the remainder consisted of soap and fat.

Mizar may be considered essentially an ointment, the chief active ingredient of which is an extract from capsicum. The ointment base is evidently a mixture of soap, petrolatum, a saponifiable fat and water.

The JOURNAL commented as follows:

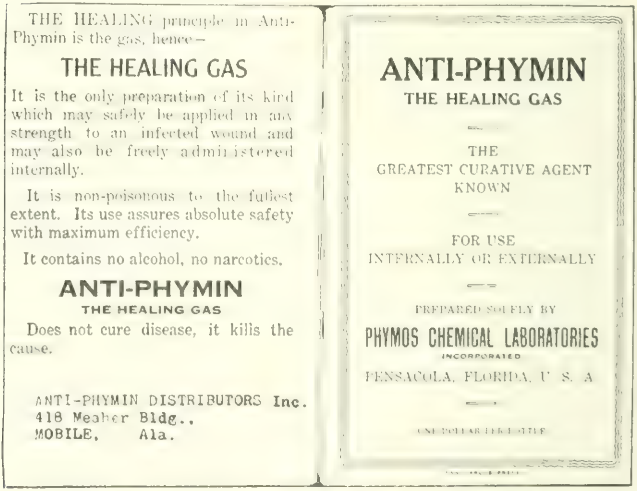
"Presumably a product of this sort appeals to those purchasers of 'patent medicine' who feel that they are not getting their money's worth unless the preparation has an appalling smell or taste or will produce some physiologic reaction that will make them sit up and take notice."

## ANTI-PHYMIN

### More Quackery of the Old Liquozone Type

*(Abstracted from The Journal A. M. A., Aug. 15, 1925, p. 535)*

Anti-Phymin, modestly described as "The Healing Gas" and the "Greatest Curative Agent Known" is at present prepared by the Phymos Chemical Laboratories of Pensacola, Florida. It is said to be "non-poisonous to the fullest extent"—whatever that means.



THE HEALING principle in Anti-Phymin is the gas, hence—

**THE HEALING GAS**

It is the only preparation of its kind which may safely be applied in any strength to an infected wound and may also be freely administered internally.

It is non-poisonous to the fullest extent. Its use assures absolute safety with maximum efficiency.

It contains no alcohol, no narcotics.

**ANTI-PHYMIN**

**THE HEALING GAS**

Does not cure disease, it kills the cause.

ANTI-PHYMIN DISTRIBUTORS Inc.
418 Meaher Bldg.,
MOBILE, Ala.

**ANTI-PHYMIN**

**THE HEALING GAS**

THE
GREATEST CURATIVE AGENT
KNOWN

FOR USE
INTERNALLY OR EXTERNALLY

PREPARED SOLELY BY

**PHYMOS CHEMICAL LABORATORIES**

INCORPORATED

PENSACOLA, FLORIDA, U. S. A

ONE DOLLAR PER BOTTLE

[illegible]

Photographic reproduction (reduced) of some of the Anti-Phymin advertising.

Nearly ten years ago the following description of the composition of Anti-Phymin was published in a booklet advertising "Cock's Camp Colony":

> "Anti-Phymin is the chemical union of allotropic oxygen, sulphurous and carbonic acid gases, bicarbonate of soda, boric acid, hypochloride of calcium, under a long continued and high degree of atmospheric pressure. Calcium water is used as a vehicle to hold the gases in solution and suspension."

Some years later (in 1921) the Anti-Phymin circular dispensed this information regarding the alleged composition of the "greatest curative agent known":

> "Anti-Phymin is a chemical union of allotropic oxygen and ozonized gases, obtained from sulphur, carbonic acid, bicarbonate of soda, boric acid, alum and hypochloride of calcium infused under super-heated atmospheric pressure with chemically affinitized water."

A bottle of Anti-Phymin prepared by the Phymos Chemical Laboratories of Pensacola, Florida, was submitted to the A. M. A. Chemical Laboratory for cursory examination. It consisted of a dilute solution of sulphurous acid and necessarily a small amount of sulphuric acid. A very small amount of residue was left on evaporation. This was not identified but it precludes the possibility of partial neutralization of the acids present.

The report indicates that Anti-Phymin belongs in the class of "Liquozone," "Radman's Microbe Killer," "Oxytonic," "Septicide," "Zymotoid" and other nostrums containing as their essential ingredient sulphurous and sulphuric acids. It will be remembered that Radman's Microbe Killer was found by the federal chemists to contain sulphur dioxide and sulphuric acid in water. Liquozone had a similar composition, as did also Oxytonic and Septicide, and still later Zymotoid. As THE JOURNAL commented, "One of the outstanding features of quackery is the lack of originality."

## ROBINSON'S PERNICIOUS ANEMIA CURE

*(Abstracted from The Journal A. M. A., Oct. 24, 1925 ,p. 1323)*

One W. A. Robinson of Sisseton, South Dakota, has been exploiting an alleged cure for pernicious anemia during the past three or four years. Original letters written by Robinson show him to be a man without any general education and his statements regarding the alleged cause and cure of pernicious anemia prove him to be utterly ignorant of medicine. According to Robinson's circulars and printed matter the "Anaemias" "never let go till they are destroyed," and that in all of his "seven months research and experimenting" he "never found but one true Anaemia, showing they never let go." Then:

> "When I had gotten the right remedy I found 450 in six days, and several hundred that had been fully destroyed. Then I began to get better and in six weeks gained fifteen pounds and could carry two buckets of water, and I never had a relapse; and now, at the age of 66, have not been as well in twenty years. It is impossible for the Anaemias to remain when my remedy is taken. My remedy is perfectly harmless."

When Robinson and his business were first brought to the attention of The Journal the thing had all the earmarks of an insignificant piece of quackery. The man's obvious illiteracy and ignorance made one feel that the public surely could never be greatly harmed by quackery of this type. As time went by, however, it became evident that sufferers from pernicious anemia were being deluded by Robinson, whose quackery, while crude, is not cheap. He charges $30 for a "treatment," which, he claims, will entirely remove the cause of pernicious anemia in twenty-five days. From letters that came in from physicians, it seemed that the main part of Robinson's "cure" was coarse sand.

In April of this year Dr. W. R. Roberts of Cissna Park, Illinois, sent in a "treatment" which one of his patients, suffering from pernicious anemia, had ordered from Robinson. The patient died, and Dr. Roberts wrote: "The end, in my opinion, was hastened by gastric disturbances induced by this treatment." The material was turned over to the Laboratory, with the suggestion that as the thing was an obvious humbug only cursory tests be made. The laboratory reported as follows:

Two bottles of a treatment for pernicious anemia purported to be exploited by W. A. Robinson of Sisseton, S. D., were subjected to a preliminary examination. One bottle contained a substance resembling coarse sand; this it was found to be; namely, sodium and potassium feldspar.

The second bottle contained a bitter-tasting, green colored liquid with suspended matter. Tests for arsenic, mercury, iron were negative; the amount of ash was less than 0.1 per cent. Alkaloids were not found. A small amount of a substance yielding an emodin reaction was present. The product is probably an aqueous solution of vegetable material (not identified) containing some chlorophyl.

In commenting on this report, The Journal stated:

"Since this report came from the Laboratory other inquiries regarding this piece of quackery have been received. The most recent is one from Dr. George Dalton of Malden, Missouri. Dr. Dalton reports that on September 8 he was called to see a patient who was suffering from pernicious anemia and had been taking Robinson's nostrum. The sand which the poor sufferer had been swallowing had caused hemorrhages which resulted in the doctor being called in. The patient died September 14.

"As Robinson's dangerous fakery is carried on exclusively through the agency of the United States mails, it is to be hoped that the efficient but overworked department that issues fraud orders will get around to Robinson before the quack gets many more victims."

## COMPATIBILITY OF CODEINE PHOSPHATE AND SODIUM BROMIDE IN SOLUTION

A query and its reply were published in THE JOURNAL, A. M. A., Sept. 26, 1925, p. 997, as follows:

*To the Editor:*—Please let me know whether codeine phosphate and sodium bromide are incompatible in solution.

G. T. C., M.D., Salt Lake City.

ANSWER:—Codeine phosphate and sodium bromide are both soluble in water; codeine hydrobromide, according to the literature, is soluble about 1 part in 80 parts of water. The A. M. A. Chemical Laboratory reports that a solution containing codeine phosphate, 2.5 per cent, and sodium bromide, 2.5 per cent, was allowed to stand several days with no apparent physical change; hence in these concentrations the two products appear to be compatible. Another solution was prepared containing codeine phosphate, 2.5 per cent (same concentration as in the previous test) and sodium bromide, 12.5 per cent (five times stronger than in the previous test). The solution was allowed to stand over night. A white crystalline precipitate was produced which formed an almost solid mass in the test tube. Tests indicated that the precipitate was codeine hydrobromide. It appears, therefore, that codeine phosphate is not compatible with sodium bromide solutions, except when the latter is in relatively low concentration.

In a solution containing codein phosphate, 2.5 per cent, and sodium chloride, 20 per cent, no precipitate was produced, which indicates that the incompatibility reported in the foregoing paragraph was due to the formation of the hydrobromide of the alkaloid and not to simple "salting out" effect.

## DR. TRIPP'S LIQUOR RHEUMATICA

### More Quackery in the Rheumatism Cure Field

*(Abstracted, with additions, from The Journal A. M. A., Oct. 30, 1925, p. 1465)*

Liquor Rheumatica is put out by a concern calling itself the Norwood Pharmaceutical Co., of Chicago.

Before putting on the newspaper campaign for the product, the concern resorted to the old method of trying to work the medical profession first. Physicians—of Chicago, at least—were circularized and urged to use Liquor Rheumatica in cases of "chronic rheumatism." No detailed information seems ever to have been given regarding the composition of the nostrum. The circular addressed to physicians vaguely mentions potassium iodide, "phytolacca-rheuma"—whatever that may be—cimicifuga and calisaya and cinchona compounds. No quantities are given except of those drugs which the federal law demands, in this instance, alcohol 12 per cent.

"Dr. John Tripp's Blood Purifier" seems to have been on the market for many years, as we have on file an advertising booklet on this product issued in 1883. At that time the preparation was put out from Buffalo, New York. In July, 1914, the Laboratory reported finding large quantities of potassium iodid with traces of cinchona alkaloids in "Dr. John Tripp's Blood Purifier." These facts should be kept in mind because of what follows:

To revert again to Liquor Rheumatica: This nostrum, after being exploited for a short time to the medical profession, was brought to the attention of the public with a flare of full-page newspaper advertisements in Chicago dailies.

Some of the claims for Liquor Rheumatica are:

> "Now there is given to the world one of the most amazing discoveries ever made by that famous medical scientist, Dr. John Tripp. It is a tried, tested and approved specific for rheumatic conditions and is called Liquor Rheumatica (Dr. Tripp)—not a patent medicine but a prescription of Dr. Tripp's which has stood most exacting tests in cases of arthritis, sciatica, gout, neuritis, myalgia, lumbago and allied conditions."
>
> "Liquor Rheumatica (Dr. Tripp) is foremost a dissolver of poisons and cleanser of the system, loosening up and dissolving the poisonous products stored up in the glands and tissues."
>
> "Try a bottle of Dr. John Tripp's Liquor Rheumatica today—banish rheumatism forever."
>
> "No case is too severe or of too long standing."
>
> "Chronic cases of many years standing, embracing all the known forms of rheumatism, have been conquered by this prescription."
>
> "Liquor Rheumatica, a prescription of the eminent scientist, Dr. Tripp, brings quick permanent relief."

Because of the number of inquiries received regarding this product, two original bottles of Dr. Tripp's Liquor Rheumatica (Norwood Pharmaceutical Co., Chicago) were submitted to the Laboratory for examination. Each bottle contained 230 cc. (approximately 7¾ fluidounces) of a liquid, with a red-brown suspension, having an aromatic odor and bitter taste. The color appeared to be due chiefly to suspended matter. On standing for some time most of the suspended matter settled, leaving an almost clear, pale reddish-yellow, supernatant liquid. The reaction was faintly acid to litmus.

No information concerning the composition of Liquor Rheumatica was given on the label of the product except that which the law requires in connection with the presence of alcohol. The label read: "Contains not more than 12 per cent alcohol." In the advertising formerly sent out by the Norwood Pharmaceutical Company, however, the presence of potassium iodide, calisaya, cinchona, cimicifuga, and "phytolacca-rheuma" were declared, although no amounts or proportions of the several ingredients were given. As calisaya is a variety of cinchona, only four drugs (in addition to alcohol) were present, according to the claims. "Phytolacca-rheuma" is not the name of any drug known to scientific medicine. Possibly the name may refer to poke root, "*Phytolacca decandra,*" which was formerly described in the Pharmacopeia of the United States.

Qualitative tests indicated the presence of alcohol, potassium, trace of sodium, trace of calcium, iodide, small amounts of cinchona alkaloids and vegetable extractives. The suspended matter was for the most part vegetable tissue and an insoluble red-brown amorphous substance. Under the microscope, the residue of vegetable tissue consisted apparently of finely powdered red saunders (*santalum rubrum*) to which substance the suspension owes its color. In fact, the vegetable residue consisted almost entirely of minute fragments of wood fibers with yellow walls; in the slightly larger masses in which one cell overlaid another, the color was more reddish. There was a trace of starch present, but nothing to indicate the starchy tissues of cimicifuga or of phytolacca root; nor were there present the needle-shaped calcium oxalate crystals of phytolacca. If extractives of these substances are present, it is probable that a fluid extract was employed. The alcohol-soluble portion of the material contained small amounts of a bitter resin. Tests for salicylates, iron, arsenic, cinchopen, colchicum, phenolphthalein, and emodin-bearing drugs, such as rhubarb, cascara and senna, were negative. Quantitative determinations were as follows:

| | |
|---|---|
| Specific gravity at 25 C. | 1.025 |
| Alcohol (by volume) | 9.3 per cent. |
| Total solids | 7.0 gm. per 100 c.c. |
| Potassium iodide | 4.2 gm. per 100 c.c. |
| Total alkaloids | 0.06 gm. per 100 c.c. |
| Water-insoluble material | 0.57 gm. per 100 c.c. |
| Water-alcohol insoluble | 0.40 gm. per 100 c.c. |
| Ether extract | 0.19 gm. per 100 c.c. |

From the foregoing examination, it is concluded that Dr. Tripp's Liquor Rheumatica is essentially a weak alcoholic solution of potassium iodide with a dash of cinchona alkaloids, to which has been added some powdered red saunders to which the product largely owes its physical appearance.

"Here, then, we have a water-alcoholic solution of potassium iodide with a dash of cinchona alkaloids advertised as 'one of the most amazing discoveries ever made by that famous medical scientist, Dr. John Tripp.' Eleven years ago when the Association's Laboratory analyzed Dr. John Tripp's Blood Purifier, which was then exploited as a cure for syphilis, the product was found to be a water-alcohol solution of potassium iodide with traces of cinchona alkaloid. From these analyses evidently Tripp's syphilis cure, alleged to have been puffed by Dr. Fred E. Stevens of Detroit, is essentially the same substance as Tripp's rheumatism cure now being puffed by Fred E. Stevens.

"The alleged 'amazing discovery' of Dr. John Tripp was neither amazing nor a discovery. For years the medical profession has used iodides in the treatment of chronic rheumatism, especially in those cases in which a syphilitic factor may be suspected. Before administering iodides, however, the physician determines whether or not these powerful drugs are contra-indicated. The purchaser of Liquor Rheumatica, of course, has no means of protecting himself against a dosing with iodides that may prove disastrous, because he is given no information regarding the presence of these drugs, and if he were, would have no knowledge of the dangers involved in their use. There is no excuse for the exploitation of a mixture such as Liquor Rheumatica in the form of a 'home remedy' for self-drugging."

## Details of Analysis

*Specific Gravity.*—The specific gravity of the preparation was taken with a pycnometer at 25 C./25 C. The weight of the liquid was 25.6294 Gm. An equal volume of water at 25 C. weighed 25.0200 Gm. This corresponds to a specific gravity of 1.0251 at 25 C./25 C.

*Solids at* 100 *C.*— Ten cc. of the well-mixed preparation were measured from a pipette into a weighed silica dish, the mixture evaporated to dryness on the steam bath and the residue dried at 100 C. From 10 cc. of the mixture a residue of 0.6902 Gm. of material was obtained, equivalent to 6.90 Gm. of solids per 100 cc. A duplicate of 10 cc. gave 0.7132 Gm. of residue, equivalent to 7.13 Gm. of solids per 100 cc. Average, 7.02 Gm. of solids per 100 cc.

*Alcohol.*—Alcohol was determined by the Official Method for Wines of the Association of Official Agricultural Chemists (Official and Tentative Methods of Analysis of the A. O. A. C., Edition 1920, p. 173). A volume of 50 cc. was distilled to 50 cc. at 15.6 C. The specific gravity of the solution was 0.9874 at 15.6 C./15.6 C. This corresponds to 9.32 per cent of alcohol by volume.

*Total Alkaloids.*—A portion of the preparation was dealcoholized on the water bath, the residue made alkaline with ammonia water and the solution shaken with successive portions of a mixture of chloroform and ether equal volumes until extraction was complete. The chloroform-ether extracts were united, and the solution shaken with successive portions of chloroform until extraction was complete. The chloroform was evaporated and the residue dried at 100 C. From 50 cc. of original material 0.0325 Gm. of total alkaloids were obtained, equivalent to 0.0650 Gm. per 100 cc. A duplicate gave 0.0330 Gm. of alkaloids, equivalent to 0.066 Gm. per 100 cc. Average, 0.0655 Gm. of total alkaloids per 100 cc.

*Potassium Iodide.*—The residue remaining in the distillation flask after the determination of alcohol was filtered, the filter thoroughly washed with warm water and after cooling the filtrate and washings made up to a volume of 500 cc. Total halide was determined by precipitating with silver nitrate solution, collecting the silver halide in a Gooch crucible, washing, drying and weighing in the usual way. The silver halide considered as silver iodide was calculated to potassium iodide. From 25 cc. of the diluted solution, equivalent to 2.5 cc. of the original material, 0.1476 Gm. of silver halide was obtained. A duplicate of 25 cc. gave 0.1481 Gm. of silver halide. Average, 0.14785 Gm. of silver halide. If considered as silver iodide, this is equivalent to 4.18 Gm. of potassium iodide per 100 cc. of original material or to 0.9868 Gm. of potassium per 100 cc. The absence of chloride and of sodium in appreciable quantities was demonstrated by the determination of potassium in aliquots of the diluted solution. A given volume of the diluted solution was evaporated to dryness and the residue ignited in presence of an excess of sulphuric acid. The residue of potassium sulphate containing a little calcium was taken up in dilute hydrochloric acid, the calcium removed by the addition of ammonium oxalate solution and ammonia water and subsequent filtration. The filtrate was evaporated to dryness, the residue moistened with sulphuric acid and heated with a fragment of ammonium carbonate.

The cooled residue was weighed. The residue was taken up in water and the solution filtered to remove traces of silica. The filtrate was evaporated and the residue heated with a drop of sulphuric acid and later with a fragment of ammonium carbonate in the usual way. The residue was considered as potassium sulphate and was calculated to potassium and to potassium iodide. The weight of potassium sulphate obtained calculated to potassium iodide amounted to very nearly the same as the weight of the silver iodide if calculated to potassium iodide. From 100 cc. of the solution a residue of 0.2162 Gm. of potassium sulphate was obtained. This is equivalent to 0.9702 Gm. of potassium for the entire sample. A duplicate of 40 cc. gave 0.0870 Gm. of potassium sulphate, equivalent to 0.9759 Gm. of potassium per 100 cc. Average, 0.9730 Gm. of potassium per 100 cc. The sulphate in one of the potassium sulphate residues was determined as barium sulphate in the usual way. The barium sulphate from 0.2162 Gm. of potassium sulphate residue gave 0.2899 Gm. of barium sulphate, equivalent to 0.2164 Gm. of potassium sulphate, equivalent to 0.9710 Gm. of potassium.

*Water-Insoluble Material.* A measured portion of the well-shaken preparation was filtered through a weighed Gooch crucible, the insoluble material washed with water and the residue dried at 100 C. to approximately constant weight. From 50 cc. of the preparation an insoluble residue of 0.2825 Gm. was obtained, equivalent to 0.5650 Gm. per 100 cc. A duplicate of 50 cc. of the preparation gave 0.2845 Gm. of water-insoluble residue, equivalent to 0.5690 Gm. per 100 cc. Average, 0.5670 Gm. of water-insoluble material per 100 cc.

*Water+Alcohol-Insoluble.*—That portion of the material insoluble in water and alcohol was determined as follows: The residue remaining in the crucible after treatment with water as described in the preceding paragraph was treated with alcohol by pouring the solvent into the crucible contained in a small beaker. The beaker was covered and allowed to stand over night. The solvent was decanted through the crucible and the residue washed several times with fresh alcohol. The residue was dried at 100 C. and weighed. From 50 cc. of the material a residue of 0.2029 Gm. was obtained which was insoluble in both water and alcohol. This is equivalent to 0.4058 Gm. of water-alcohol insoluble material. A duplicate of 50 cc. gave 0.1971 Gm. of water-alcohol insoluble material, or 0.3942 Gm. per 100 cc. Average, 0.4000 Gm. of water-alcohol insoluble material per 100 cc.

# PART III

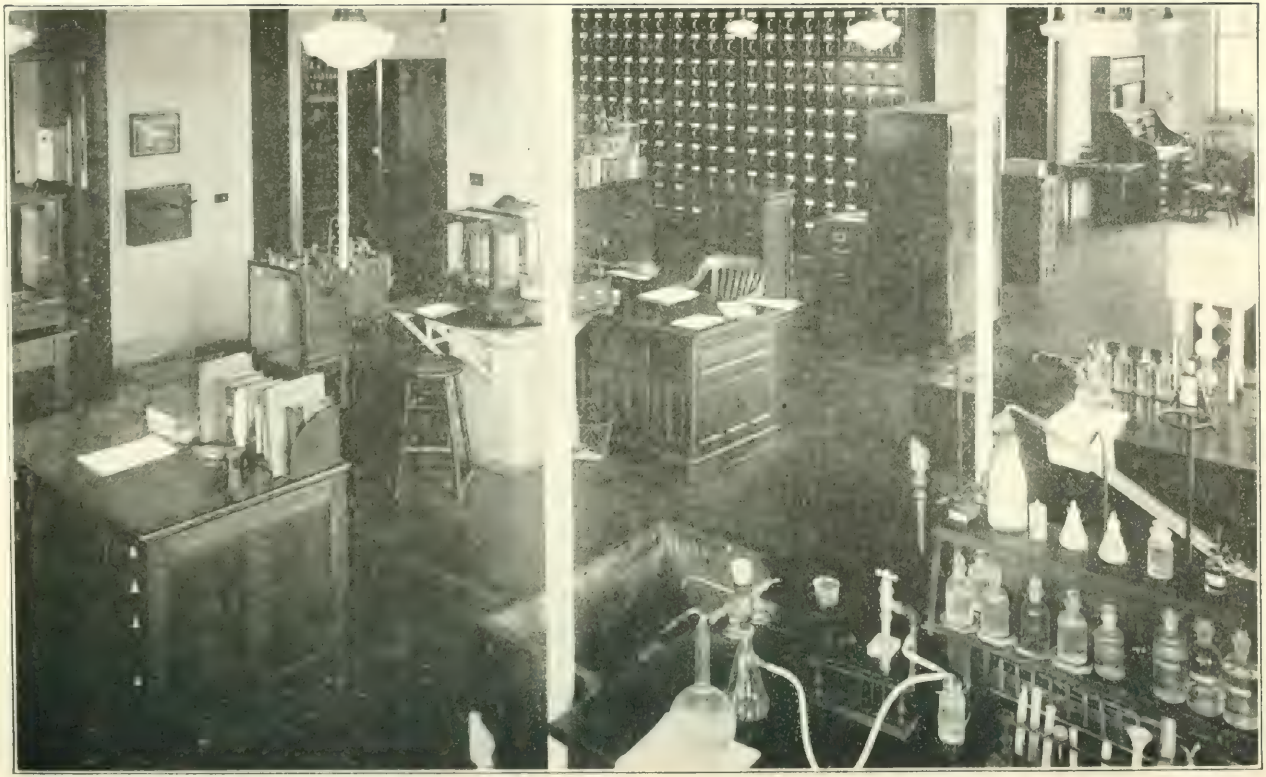
## REPORTS NOT PREVIOUSLY PUBLISHED

### THE NEW QUARTERS OF THE A. M. A. CHEMICAL LABORATORY

Shortly after the Council on Pharmacy and Chemistry was organized, the Trustees created the Chemical Laboratory as an aid to the Council. Primarily it is engaged in checking up the composition and properties of proprietary and nonofficial remedies. Also, nostrums exploited to the public are analyzed, and through the columns of THE JOURNAL or by direct correspondence, physicians are furnished with information on diversified medicochemical subjects.

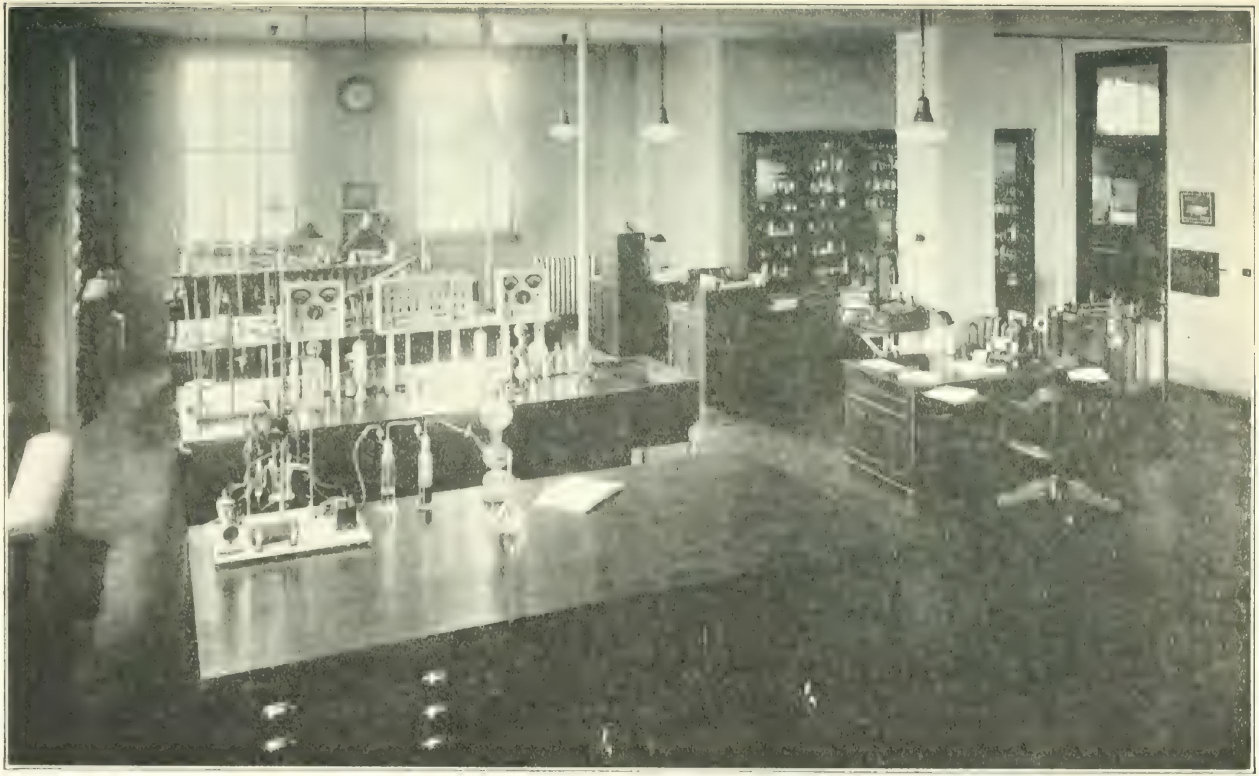
The Chemical Laboratory is located in the northeast portion of the fifth floor of the A. M. A. Headquarters Building. In 1924 it moved to these new quarters, which were built according to specifications supplied by the Laboratory staff. On entering the new Laboratory, one finds a well lighted room with windows on three sides and adequate provision for artificial light on dark days. There are no unsightly pipes or ugly electrical conduits so common in most laboratories; water, gas and drain pipes are concealed in concrete troughs with removable floor covers. The Laboratory has been adequately wired by means of concealed conduits for electricity in order to provide for future needs, and outlets have been distributed so that current may be available on any work table or other advantageous location.

Just inside the door, to the left, is the stock room for chemicals, drugs and glassware; from this point will also be noticed a large steel filing cabinet in which has been kept specimens of any drug or chemical that has been brought to the attention of the Laboratory or the Council. One of the greatest assortments of proprietaries existing will be found here, carefully indexed for future comparison. Turning to the right, one enters the fume room; here are constant temperature ovens, and a large fume cabinet connected with a powerful fan on the roof. The cabinet is provided with lights, electric current, water and gas. Adjacent to it is the



A. M. A. CHEMICAL LABORATORY

At left, entrance to stock room; in middle background, steel filing case for specimens.



A. M. A. Chemical Laboratory

At left, work tables; at right, entrance to fume and oven room and to dark room.

leadlined steam cabinet, which is connected directly with the boiler room. Along the east wall of the room are electric and steam stills for preparing distilled water, the centrifuge with an unusual safety control feature, and a large sink for cleaning dishes (a work that keeps a laboratory assistant occupied most of his time); also there are asbestos slate top tables on which blast lamps and heavy electrical heating apparatus may be used. Adjacent to this room is a small dark room equipped with polariscope, spectroscope, colorimeter, etc.

The main laboratory room contains a large constant temperature water bath for artificial digestion experiments; efficiently arranged cases for chemical reagents; weighing tables, balances, and modern equipment. Here are four large, well equipped laboratory work desks (besides a storage desk). On one is permanently fixed a delicate electrolytic outfit for determination of metals; on another is kept the hydrogen ion apparatus, so essential now to a modern laboratory. In the laboratory is also a fireproof safe with individual compartments where specimens may be kept while undergoing analysis. In the west end of the main room is located the office of the Secretary of the Council; the card index files (containing about 75,000 cards on chemotherapeutic subjects) and the stenographic force. Nearby one enters the departmental library, which is constantly used in formulating replies to inquiries and for reference work for both the Council and the Laboratory. The current literature rack shows that the Laboratory receives monthly about fifty foreign and domestic publications in the field of chemisry, pharmacy and related biosciences, and this information is made available to physicians. Furthermore, the extensive current literature permits prompt indexing of new remedies and also serves to keep the chemists informed on the newer methods of investigation.

The last point of interest is the good sized record room, devoted mainly to the Council. Advertisements, circular letters, "boost" articles on new therapeutic agents and information on patents are filed here. For each large firm there is a separate envelop containing material regarding each proprietary remedy. In this room are also kept reprints of Council or Laboratory articles which will serve as replies to inquiries. Finally, all the correspondence since 1905 has been indexed and bound in volumes. This serves as a means of protection against garbling of statements by unscrupulous promoters and as a ready means of reference for use of the Council.

The personnel of the Laboratory includes Dr. Paul N. Leech, director of the Laboratory; Dr. Joel B. Peterson, chemist; Dr. George W. Collins, chemist; Miss Violette Svoboda, secretary, and Mr. Earl J. Adams, laboratory assistant. From time to time investigators in chemistry of materia medica are given the courtesy of taking special work in the A. M. A. Chemical Laboratory.

## AGAR FLAKES (AMERICAN AGAR COMPANY)

### Opinion Given at Request of the Council

The Council on Pharmacy requested the opinion of the Laboratory on the report by the Medical Research Laboratories of their examination of Agar Flakes (American Agar Company).

The report of the Medical Research Laboratories showed that one specimen each of three brands (besides the Agar Flakes) were investigated, Parke, Davis & Co., Lehn & Fink, and Merck & Co. The determinations were on:

1. Moisture.—The variations were not important.

2. Ash.—The variations were not important, Agar Flakes being the highest.

3. Water Soluble Material.—Varied from 16 to 25 per cent (Agar Flakes was 19.6 per cent).

4. Therapeutically Active Material (remainder after subtracting sum of 1, 2 and 3). Variation unimportant.

5. A. Water Imbibing Power in cc. (from 1 Gm.):

| | |
|---|---|
| P. D. & Co | 21 |
| Am. Ag. Co | 29 |
| L. & F | 20 |
| Merck | 12½ |

B. Swelling Power in cc.:

| | |
|---|---|
| P. D. & Co | 37½ |
| Am. Ag. Co | 46 |
| L. & F | 33½ |
| Merck | 12½ |

6. Viscosity 1 per Cent "Solution":

| | Time in Minutes |
|---|---|
| P. D. & Co | 1.18 |
| Am. Ag. Co | 1.46 |
| L. & F | 1.30 |
| Merck | 1.21 |
| Water | 0.96 |

7. Gold Test.—Was unimportant, the Agar Flakes and P. D. & Co. being poorest.

The report brings out the fact that other brands of Agar Agar are also starchless as are the Agar Flakes (American Agar Company).

The differences in the findings for the water imbibing power as reported by the Medical Research Laboratories are in favor of Agar Flakes, but such tests can probably be made to vary according to conditions.

The A. M. A. Chemical Laboratory points out that in the tests of water imbition made by the Medical Research Laboratories, the comparison of Agar Flakes (American Agar Company) was not made with flakes of another product, but evidently with coarse forms of agar. In view of this the Laboratory carried out an experiment as described by the Medical Research Laboratories * (except the water was at room temperature), using Agar Flakes, P. D. & Co. as control. After 19 hours Agar Flakes (Am. Agar Co.) absorbed 210 cc. of water. Agar Flakes P. D. & Co. absorbed 215 cc. of water. This indicates (as far as this single experiment goes) that one brand of flakes is not superior to the other in reference to the water imbibing factor. When Merck Shreds were used, for comparison, both brands of *flakes* showed considerably better water imbibing power. Of course the test as devised by the Medical Research Laboratories is only roughly indicative of water absorption in vito.

It is the opinion of the American Medical Association Chemical Laboratory that the evidence for Agar Flakes (American Agar Co.) does not warrant a conclusion that the product is sufficiently superior to other brands on the market to justify recognition by the Council on claims of chemical superiority alone.

## AIROL

Airol (Hoffmann LaRoche Chemical Works, New York) is stated to be bismuth oxyiodogallate. Recently the product was resubmitted for inclusion in New and Nonofficial

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* The method used by the Medical Research Laboratories for determining the water imbibing capacity was as follows:

Ten grams of agar were left in contact with 600 cubic centimeters of distilled water at body temperature, 37½ degrees Centigrade, in a liter beaker. The contents of the beaker were then transferred to a washed cheesecloth spread over a six inch funnel, and allowed to drain five minutes. The liquid which came through the cheesecloth was measured and when deducted from six hundred gave the number of cubic centimeters of water imbibed by ten grams of agar.

Remedies. Accordingly the Laboratory was asked to draw up a proposed description; in this connection several preliminary tests were made.

According to a letter from the manufacturer, evidence of liberation of iodine is the quotation from the nineteenth edition of the U. S. Dispensatory.

> "When airol is brought in contact with surgical secretions it becomes red from the liberation of iodine. According to the researches of Carl S. Haegler (Beitrage zur klin. Chir., Vol. xv, p. 1, 1896), it is about as feeble a germicide as is iodoform, but as in the case of iodoform the substances liberated by its decomposition in wounds are actively germicidal."

The firm also referred to the statement in N. N. R., 1923, that Airol is practically insoluble in water, but communicates to the water a red coloration on standing, being decomposed with liberation of iodine and bismuth subgallate.

The following preliminary observations were noted:

(1) A sample of Airol (from the specimen sent in by the manufacturer) was treated with water (1 part airol to 100 parts water) and permitted to stand over night. No red color was present. The centrifuged solution was clear and colorless and when shaken with chloroform gave no evidence of free iodine being present. When treated with ferric chloride, however, iodine was liberated showing that iodide ($I^-$) was present. The insoluble material in the aqueous solution was composed of two distinct layers, one yellow, and the other grayish black.

(2) When the dry powder was placed on a filter paper and washed with water, the clear filtrate did not contain iodine, but did contain a relatively large amount of a substance having the reactions of an iodide.

(3) According to the tests, Airol is insoluble in alcohol. When an alcoholic suspension of Airol was filtered, the filtrate did not contain free iodine, but did respond to tests for iodide. The residue, which was washed well with alcohol, was dissolved in diluted nitric acid. No iodide was present in the solution; tests for bismuth were positive.

The observations were sent to the manufacturer with the comment: "These tests made on the specimen received indicate that free iodine is not liberated from Airol; that the therapeutic value of Airol probably is independent of the iodine content, and that the composition of Airol is not in accordance with the claims."

In its reply to the Council on Pharmacy and Chemistry, the manufacturer stated that in order to expedite matters, specimens were inadvertently sent from a lot purchased from an American manufacturer who claimed to produce a product equivalent to Airol. The firm asked that the question of the chemistry of Airol be held in abeyance until "we write to you again on the subject which will be shortly." As considerable time has elapsed since this correspondence, and as the firm is not advertising the product, these observations are published solely as a matter of record.

## ANTIMONY THIOGLYCOLLAMIDE AND ANTIMONY SODIUM THIOGLYCOLLATE

A specimen each of antimony thioglycollamide and antimony sodium thioglycollate was submitted to the Laboratory for examination and confirmation of the submitted statements of composition.

### Antimony Thioglycollamide

The specimen of antimony thioglycollamide was a white, crystalline, odorless powder; somewhat soluble in water and in alcohol.

*Loss on Drying.*—A weighed specimen was dried first over sulphuric acid and afterward at 100 C. in a drying oven. The loss from 0.2271 Gm. was 0.0004 Gm. over sulphuric acid, equivalent to 0.176 per cent. At 100 C. the additional loss was 0.0001 Gm., equivalent to 0.044 per cent. Total loss 0.22 per cent. Since the loss on drying was so insignificant a duplicate determination was not made.

*Antimony.*—Antimony was determined by the following method:

> Weigh accurately from 0.2 to 0.3 Gm. of antimony thioglycollamide, dissolve in about 100 cc. of warm water, add 1 cc. of diluted hydrochloric acid, pass in hydrogen sulphide until precipitation is complete and allow to stand 30 minutes. Collect the antimony sulphide in a weighed Gooch crucible, wash successively with water containing hydrogen sulphide, alcohol, ether, carbon disulphide, alcohol and ether, dry at 110 C. and weigh. The antimony sulphide obtained should correspond to not less than 30 per cent of antimony.

The antimony sulphide from 0.2761 Gm. of material weighed 0.1262 Gm., equivalent to 32.65 per cent of antimony. The antimony sulphide from 0.2271 Gm. of material weighed 0.1039 Gm., equivalent to 32.67 per cent of antimony. Average, 32.66 per cent of antimony. The theory for the formula $Sb(SCH_2CONH_2)_3$ is 30.77 per cent of antimony. These results were submitted to the manufacturer. The manufacturer reported that a specimen of antimony thioglycollamide was thrice crystallized and the antimony in the purified compound determined by the firm's chemist, Dr. Daniel Base. He reported the antimony content as 32.27 per cent. This is slightly lower than was found in the Association's Laboratory, but the value is still considerably above that required by the theoretical formula.

Based for the most part upon information furnished by the manufacturer, but to some extent upon the results of the examination obtained in the Association's Laboratory, the following description of antimony thioglycollamide was prepared for New and Nonofficial Remedies:

> Antimony thioglycollamide is a white, crystalline, odorless powder. It is soluble in about 200 parts of water; somewhat soluble in alcohol; insoluble in ether. It melts at about 139 C. (uncorrected).
>
> Dissolve a few crystals of antimony thioglycollamide in 5 cc. of water and add a drop of ferric chloride solution; a transient blue color appears. Boil about 0.1 Gm. of antimony thioglycollamide with 5 cc. of sodium hydroxide solution; ammonia is evolved. Dissolve about 0.1 Gm. of antimony thioglycollamide in 25 cc. of warm water, add a few drops of diluted hydrochloric acid and pass in hydrogen sulphide; an orange precipitate is produced.
>
> Dissolve 0.2 Gm. of antimony thioglycollamide in 5 cc. of hydrochloric acid, add 10 cc. of freshly prepared stannous chloride solution and allow to stand 30 minutes. No brownish tint or precipitate should be visible if viewed from above over a white surface (*arsenic*). A blank test should be carried out, using the same quantities of reagents.
>
> Weigh accurately from 0.2 to 0.3 Gm. of antimony thioglycollamide, dissolve it in about 100 cc. of warm water, add 1 cc. of diluted hydrochloric acid, pass in hydrogen sulphide until precipitation is complete and allow to stand 30 minutes. Collect the antimony sulphide in a weighed Gooch crucible, wash it successively with water containing hydrogen sulphide, alcohol, ether, carbon disulphide, alcohol and ether, dry the residue at 110 C. and weigh. The antimony sulphide obtained corresponds to not less than 30 per cent of antimony.

## ANTIMONY SODIUM THIOGLYCOLLATE

Loss on drying was determined by drying over sulphuric acid and afterward by drying in an air oven at 100 C. The loss over sulphuric acid from 0.3064 Gm. was 0.004 Gm., equivalent to 0.13 per cent. The loss at 100 C. after sulphuric acid amounted to 0.007 Gm., equivalent to 0.23 per cent. Total loss is 0.36 per cent. As the loss was very small a duplicate determination was not carried out.

*Antimony.*—Antimony was determined by the method given under antimony thioglycollamide. The antimony sulphide obtained from 0.225 Gm. of material weighed 0.1326 Gm., equivalent to 37.53 per cent of antimony. A duplicate of 0.2928 Gm. gave 0.1525 Gm. of antimony sulphide, equivalent to 37.20 per cent of antimony. Average, 37.36 per cent of antimony. Based largely upon information furnished by the manufacturer, but partially upon the results obtained in the chemical examination, the following description was prepared for New and Nonofficial Remedies:

> Antimony sodium thioglycollate is a white or faintly pinkish powder; odorless or having a faint odor of mercaptan; very soluble in water; insoluble in alcohol.
>
> Add a drop of diluted hydrochloric acid to 3 cc. of a dilute solution of antimony sodium thioglycollate (1-100) and add two drops of 1 per cent ferric chloride solution. A transient blue color results. Add a drop of 1 per cent ammonia water to this mixture and shake. A Bergundy red color results. Add a few drops of sodium hydroxide solution to a dilute solution of antimony sodium thioglycollate (1-100); a white precipitate is produced. Dissolve about 0.1 Gm. of antimony sodium thioglycollate in 2 cc. of water, add a few drops of diluted hydrochloric acid and pass in hydrogen sulphide; an orange colored precipitate is produced.
>
> Weigh accurately from 0.2 to 0.3 Gm. of antimony sodium thioglycollate, dissolve it in about 100 cc. of warm water, add 1 cc. of diluted hydrochloric acid, pass in hydrogen sulphide until precipitation is complete and allow to stand 30 minutes. Collect the antimony sulphide in a weighed Gooch crucible, wash it successively with water containing hydrogen sulphide, alcohol, ether, carbon disulphide, alcohol and ether, dry the residue at 110 C. and weigh. The antimony sulphide corresponds to not less than 37 per cent of antimony.

## BISMUTH SALICYLATE IN OIL, P. D. & CO.

Three original bottles of Bismuth Salicylate in Oil, Parke, Davis & Co., were submitted to the Laboratory for determination of bismuth content. The preparation was a yellow-gray suspension, having an odor of camphor and creosote. Two specimens, A and B, were mixed and used for the bismuth determination. It was found practically impossible to obtain strictly uniform specimens, due to "settling out."

According to the circular, accompanying the package, one cc. contains 2 grains (0.130 Gm.) of bismuth salicylate. The specific gravity at 25 C. of one specimen was 1.019. (This is considered closely aproximate.) The preparation was assayed for bismuth oxide according to the ignition method of U. S. P. X, and calculations based on the assumption that the bismuth salicylate yielded the minimum amount of bismuth oxide ($Bi_2O_3$) permitted by the U. S. P. X (i. e., 62 per cent).

Four determinations were made; the following figures show the percentage of the amount claimed to be present:

| | |
|---|---|
| A | 96.1 per cent |
| B | 97.8 per cent |
| C | 100.2 per cent |
| D | 99.6 per cent |

Average 98.4 per cent of the amount claimed. The pharmacopeia assay method also permits a maximum amount of bismuth oxide, i. e., 66 per cent. Based on this, the average of the maximum claimed amount is 104.9 per cent. The mean value is 101.6 per cent.

*Conclusions.*—The bismuth content of "Bismuth Salicylate in Oil, Parke, Davis & Co." was found to be very close to the amount claimed.

## GLASEPTIC AMPOULES BISMUTH SALICYLATE IN OIL, P. D. & CO.

Three original packages of Glaseptic Ampoules Bismuth Salicylate in Oil—Parke, Davis & Co. were submitted to the Laboratory for examination. Each ampoule is claimed to contain 1 cc. of material; each cc. of the product was stated to contain 2 grains (0.130 Gm.) of bismuth salicylate. The contents of four ampoules were found to be 1.225 Gm., 1.239 Gm., 1.246 Gm. and 1.238 Gm., corresponding respectively to 1.20 cc., 1.22 cc., 1.22 cc. and 1.22 cc. The preparation was assayed for bismuth oxide according to the ignition method of the U. S. P. X, and calculations based on the assumption that the bismuth salicylate yielded the minimum amount of bismuth oxide ($Bi_2O_3$), permitted by the U. S. P. X (i. e., 62 per cent).

Three determinations were made. The following figures show the per cent found of the amount claimed:

| | |
|---|---|
| A | 98.67 per cent |
| B | 100.1 per cent |
| C | 100.1 per cent |

Average 100.0 per cent.

The U. S. P. assay method also permits a maximum amount of bismuth oxide, i. e., 66 per cent. Based on this, the average of the amount found as compared to the amount claimed is 106.6. The mean value is 103.3 per cent.

*Conclusions.*—The bismuth content of Glaseptic Ampoules Bismuth Salicylate in Oil, Parke, Davis & Co. was found to be very close to the amount claimed.

## TRIBASIC CALCIUM AND MAGNESIUM PHOSPHATES

**By Joel B. Peterson, Ph.D.**

The Powers-Weightman-Rosengarter Company of Philadelphia submitted to the Council on Pharmacy and Chemistry of the American Medical Association a sample of Magnesium Phosphate Tribasic and a sample of Calcium Phosphate Tribasic. These specimens were turned over to the A. M. A. Chemical Laboratory for examination. As this was the first time products of this kind had been examined by the Laboratory it was thought advisable for purposes of comparison to examine other products of this type that are being sold. Accordingly there were bought in the open market a specimen of Triophos prepared by Lehn and Fink, Inc., of New York, and a specimen of Precipitated Calcium Phosphate which is distributed by Schieffelin and Co., of New York. Of these two products the former is purported to be a mixture of the tertiary phosphates of magnesium and calcium and the latter is a National Formulary (IV) product. *Calcii Phosphas Praecipitatus* is described in the National Formulary as being the tertiary phosphate of calcium.

Each of the products examined proved to be a fine, white powder, insoluble in neutral or alkaline solution. The Tribasic Magnesium Phosphate of the Powers-Weightman-Rosengarten Co. was entirely soluble in dilute acid. The other three specimens contained a small amount of acid-insoluble material. Triophos of Lehn and Fink, Inc., had a slight odor of menthol. The other three specimens were odorless. Both products labeled calcium phosphate contained small amounts of aluminum compounds as a contaminant; these were not found in the magnesium products.

It should be pointed out that it is possible to prepare a mixture of secondary calcium phosphate and calcium oxide or carbonate that will give practically the ratio of calcium to phosphate in tertiary calcium phosphate.

It was, therefore, necessary to determine the carbonate content and the carbon dioxide absorbing power of the products. These and the other quntitative data are recorded in the following table.

| | Calcium Phosphate Tribasic Powers-Weightman-Rosengarten Co. | Magnesium Phosphate Tribasic Powers-Weightman-Rosengarten Co. | Triophos Lehn and Fink | Precipitated Calcium Phosphate N. F. Schieffiin & Co. |
|---|---|---|---|---|
| Loss on heating at 200 C.*.. | 4.46 | 18.51 | 15.86 | 5.10 |
| $Ca^{++}$ | 34.42 | ..... | 9.56 | 33.98 |
| $Mg^{++}$ | ..... | 20.29 | 13.68 | ..... |
| $PO_4^{---}$ | 51.90 | 53.87 | 50.75 | 53.12 |
| $PO_4^{---}$ calculated from Ca and Mg content | 52.78 | 52.52 | 48.74 | 52.52 |
| $SO_4^{--}$ | 0.97 | ..... | 0.83 | 1.09 |
| $CO_3^{--}$ | 0.95 | 0.34 | 1.42 | 0.47 |
| MgO | ..... | 0.27 | ..... | ..... |
| CaO * | 0.39 | ..... | 0.93 | 0.49 |
| Acid insoluble* | Trace | None | 0.33 | 0.22 |

* One determination.
All values are reported in per cent.

From the foregoing, it apears that the four products do contain the important constituents in ratios that are practically correct for the compounds claimed by the manufacturers. Only small amounts of carbonate and oxide were found.

The can in which Triophos came bore a label on which an analysis was printed. It totaled 100 per cent but the figures did not agree with those recorded in this report and were obviously incorrect. Exclusive of Triophos the preparation containing basic magnesium phosphate was found to contain about 74 per cent of free anhydrous tribasic phosphate and those that do not contain magnesium contain about 86 per cent of anhydrous calcium tribasic phosphate.

It will be noted that these tests limit the amount of calcium carbonate and uncombined calcium oxide. As the products were not very pure (88 to 94 per cent) it was necessary to determine the phosphate, to limit the amount of dibasic material, and to determine the cation and to calculate its ratio to the theoretical amount of phosphate ($PO_4^{---}$) present. This latter figure, if the product is mainly tribasic, should be within a reasonable per cent of the actual $PO_4^{--}$ found. Based on this, tests were drawn up.

The analytical work, together with proposed tests were submitted to the manufacturer. After considerable correspondence, and a number of excellent suggestions from Dr. Rosin of the Powers-Weightman-Rosengarten Company, the Laboratory elaborated the following standards for New and Nonofficial Remedies:

**TRIBASIC CALCIUM PHOSPHATE.**—Calcii Phosphas Tribasicus.—Tertiary Calcium Phosphate, $Ca_3(PO_4)_2$. Tribasic calcium phosphate contains approximately 85 per cent of $Ca_3(PO_4)_2$.

Tribasic calcium phosphate occurs as a white, odorless and tasteless powder. It is almost insoluble in water but is readily soluble in diluted mineral acids. Water agitated with tribasic calcium phosphate is neutral or acquires a slight alkaline reaction to litmus paper.

Dissolve 0.2 Gm. of tribasic calcium phosphate in 5 cc. of diluted hydrochloric acid, add drop by drop ammonia water until a precipitate forms, add 1 cc. of acetic acid, followed by 1 or 2 cc. of ammonium oxalate solution: a white precipitate forms. Dissolve 0.2 Gm. of tribasic calcium phosphate in a slight excess of diluted nitric acid and add ammonium molybdate solution: a yellow precipitate forms which is soluble in ammonia water. Mix 0.2 Gm. of tribasic calcium phosphate with about 5 cc. of water, then add 20 cc. of neutral solution of silver nitrate (1 in 20) and agitate the mixture for about two minutes, keeping protected from light: the liquid is neutral to litmus paper (*distinction from dibasic phosphate*), and the precipitate is of a pure yellow color, free from brown or gray (*uncombined calcium oxide*). A solution of 0.2 Gm. of the salt in 10 cc. of water and just sufficient hydrochloric acid is not darkened by the addition of an equal volume of hydrogen sulphide water (*heavy metals*). Mix 0.5 Gm. of the salt with 3 cc. of water and immediately add 3 cc. of diluted hydrochloric acid: not more than a few gas bubbles should be evolved (*carbonate*). Dissolve 0.2 Gm. of tribasic calcium phosphate in 10 cc. of diluted nitric acid and add 1 cc. of silver nitrate solution: not more than a slight turbidity results (*chloride*). To a solution of 0.5 Gm. of the salt in 10 cc. of diluted hydrochloric acid, filtered if necessary, add a few drops of diluted sulphuric acid: no turbidity is produced in ten minutes (*barium*). Dissolve 0.2 Gm. of tribasic calcium phosphate in 5 cc. of diluted nitric acid, add a few cubic centimeters of sulphuric acid and heat until fumes of sulphur trioxide are evolved; add 10 cc. of sulphurous acid solution, evaporate until the solution is free from sulphur dioxide, dilute the evaporated solution to 5 cc.: this meets the U. S. P. X limit for arsenic. Digest 2 Gm. of the salt with 100 cc. of water for one-half hour on a steam bath, cool, add sufficient water to restore the original volume, stir well, filter, evaporate 50 cc. of the filtrate to dryness in a porcelain dish, and ignite the residue gently: the weight of the residue does not exceed 0.005 Gm. (*soluble salts*). Dissolve 0.2 Gm. of tribasic calcium phosphate in the smallest possible amount of diluted hydrochloric acid, filter, wash, make the filtrate up to 49 cc. and add 1 cc. of barium chloride solution: the turbidity produced should not be greater than is apparent in a similarly made up control tube using 2 cc. fiftieth-normal sulphuric acid in place of the calcium phosphate (see U. S. P. X, page 462). Agitate 1 Gm. of tribasic calcium phosphate with 30 cc. water for five minutes, filter and add to the filtrate 2 drops phenolphthalein solution: the pink color, if any, is completely discharged by one drop of tenth-normal acid (*uncombined calcium oxide*).

Dissolve about 0.2 Gm. tribasic calcium phosphate, accurately weighed, in a mixture of 25 cc. of water and 10 cc. nitric acid, filter and wash if not entirely soluble, add ammonia water until a slight precipitate is produced, then dissolve the precipitate by the addition of 1 cc. of nitric acid, cool or heat the solution to about 50 C., add 75 cc. of ammonium molybdate solution, and allow to remain at this temperature for thirty minutes, stirring occasionally, filter at once, wash once or twice with water by decantation, using 30 to 40 cc. each time, transfer the precipitate to the filter and wash with cold water until the washings cease to react acid with litmus paper, transfer the precipitate and filter to the precipitating vessel, add 50 cc. of half-normal sodium hydroxide, agitate until the precipitate is dissolved and then titrate the excess of alkali with half-normal sulphuric acid, using 3 drops of phenolphthalein solution as indicator. Each cubic centimeter of half-normal sodium hydroxide consumed corresponds to 0.002066 Gm. $PO_4{\equiv}$. The amount of phosphate ($PO_4{\equiv}$) should not be less than 52 per cent.

Dissolve about 0.5 Gm. of tribasic calcium phosphate, accurately weighed, in diluted hydrochloric acid; filter if the product is not entirely soluble, wash, and add ammonia water until a permanent precipitate just forms; add 2 per cent citric acid solution until the precipitate just dissolves and then add 50 cc. more; make up to 200 cc.; add an excess of ammonium oxalate solution, allow to stand one hour on the steam bath, filter, wash, dissolve the precipitate in diluted hydrochloric acid, then add ammonia water until alkaline, and a few cubic centimeters of ammonium oxalate solution; allow the mixture to stand on the steam bath an hour, filter, wash, dry and ignite to constant weight; calculate the weight of the calcium oxide to calcium (Ca): the percentage of calcium found multiplied by the factor 1.581 (Ca to $PO_4{\equiv}$ in $Ca_3(PO_4)_2$) should correspond with the percentage of phosphate ($PO_4{\equiv}$) found plus or minus 2.5 per cent.

On ignition, tribasic calcium phosphate loses not more than 8 per cent of its weight.

**TRIBASIC MAGNESIUM PHOSPHATE.** — Magnesii Phosphas Tribasicus.—Tertiary Magnesium Phosphate, $Mg_3(PO_4)_2.7H_2O$. Tribasic magnesium phosphate contains approximately 70 per cent $Mg_3(PO_4)_2$.

Tribasic magnesium phosphate occurs as a white, odorless and tasteless powder. It is almost insoluble in water, but it is readily soluble in diluted mineral acids. Water agitated with tribasic magnesium phosphate is neutral or acquires a slightly alkaline reaction to litmus paper.

Dissolve about 0.2 Gm. of tribasic magnesium phosphate in a slight excess of diluted nitric acid and add ammonium molybdate solution: yellow precipitate forms which is soluble in ammonia water. Mix 0.2 Gm. of tribasic magnesium phosphate with about 5 cc. of water, then add 20 cc. of neutral solution of silver nitrate (1 in 20) and agitate the mixture for about two minutes, keeping protected from light: the liquid is neutral to litmus paper (*distinction from dibasic phosphate*), and the precipitate is of a pure yellow color, free from brown or gray (*uncombined magnesium oxide*). A solution of 0.2 Gm. of the salt in 10 cc. of water and just sufficient hydrochloric acid is not darkened by the addition of an equal volume of hydrogen sulphide water (*heavy metals*). Mix 0.5 Gm. of the salt with 3 cc. of water and add 3 cc. of diluted hydrochloric acid: not more than a few gas bubbles should be evolved (*carbonate*). Add 5 cc. of sodium hydroxide solution to 0.5 Gm. of tribasic magnesium phosphate solution and heat: the odor of ammonia is not evolved (*magnesium ammonium phosphate*). To a solution of 0.5 Gm. of the salt in 10 cc. of diluted hydrochloric acid, filtered if necessary, add a few drops of diluted sulphuric acid: no turbidity is produced in ten minutes (*barium*). Dissolve 0.2 Gm. of tribasic magnesium phosphate in 5 cc. of diluted nitric acid, add a few cubic centimeters of sulphuric acid and heat until fumes of sulphur trioxide are evolved; add 10 cc. of sulphurous acid solution, and evaporate until the solution is free from sulphur dioxide; dilute the evaporated solution to 5 cc.: this meets the U. S. P. X limits for arsenic. Add 30 cc. of water to 1 Gm. of the salt; follow with 5 cc. of hydrochloric acid, warm if necessary until the salt is dissolved, cool, add ammonia water in small portions until a permanent precipitate is just produced and then add 5 cc. acetic acid: not more than a slight quantity remains undissolved (*aluminum, iron, etc.*). Filter the solution if not clear and add 5 cc. ammonium oxalate: not more than a slight turbidity is produced (*calcium*). Dilute 1 cc. of the solution to 200 cc. and add ammonia water until alkaline to litmus paper: a white crystalline precipitate gradually appears. When tribasic magnesium phosphate is assayed for chloride and sulphate according to the method described in the U. S. P. X, page 462, their sum should not exceed 0.5 per cent. Digest 2 Gm. of the salt with 100 cc. of water for one-half hour on a steam bath, cool, add sufficient water to restore the original volume, mix and filter; evaporate 50 cc. of the filtrate to dryness and ignite gently: the weight of the residue does not exceed 0.015 Gm. (*soluble salts*). Agitate 1 Gm. of tribasic magnesium phosphate with 20 cc. of water for five minutes, filter, and add to the filtrate 2 drops phenolphthalein solution: the pink color, if any, is completely discharged by one drop of tenth-normal acid (*uncombined magnesium oxide*).

Determine the phosphate content of tribasic magnesium phosphate by the method given under tribasic calcium phosphate. The amount of phosphate ($PO_4^{\equiv}$) should not be less than 50 per cent.

Dissolve about 0.5 Gm. of tribasic magnesium phosphate, accurately weighed, in 25 cc. of diluted hydrochloric acid; add ammonia water in small portions until a permanent precipitate is just produced and redissolve the precipitate by the addition of acetic acid; if the solution is not clear, filter and wash; add to the solution 10 cc. of sodium phosphate T. S., then render strongly alkaline by the addition of stronger ammonia water; allow the mixture to stand twenty-four hours; filter on a tared Gooch crucible and wash the precipitate with diluted ammonia water (1 volume of ammonia water diluted with 19 volumes of water) until the washings cease to give a reaction for chloride, ignite and weigh: the percentage of magnesium found multiplied by 2.605 (factor Mg to $PO_4^{\equiv}$ in $Mg_3(PO_4)_2$) should correspond to the percentage of phosphate ($PO_4^{\equiv}$) found plus or minus 1.5 per cent.

On ignition it loses from 25 per cent to 30 per cent of its weight.

## Details of Analysis

*Calcium.*—About 0.5 Gm. sample of the preparation accurately weighed was dissolved in the smallest possible amount of diluted hydrochloric acid. The solution was filtered and the filter washed with water. A 50 cc. portion of 2 per cent citric acid solution and later an excess of ammonium oxalate solution were added. After standing several hours the solution was filtered and the filter washed with water. The filter was pierced and the precipitate washed into a clean beaker. The precipitate was dissolved in diluted hydrochloric acid and then a new precipitate was formed by making alkaline with ammonia water and adding an excess ammonium oxalate. After the solution had been allowed to stand on the water bath for an hour it was filtered. The filter was washed with water. It was transferred to a platinum crucible, dried in the oven at 100 C. for an hour and then blasted to constant weight and weighed as calcium oxide.

There was one difference from the above procedure for the determination of calcium in Triophos. The preparation was dissolved in the smallest amount of diluted hydrochloric acid, filtered and the filter washed. Ammonia water was added until a slight permanent precipitate formed. A 2 per cent citric acid solution was then added until the precipitate dissolved and then 50 cc. more was added. The remainder of the procedure was just as has been described.

*Calcium Phosphate Tribasic. P. W. R. Co.*—A sample weighing 0.6153 Gm. gave 0.2977 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 34.57 per cent of calcium $\mathrm{Ca}^{++}$). A sample weighing 0.8654 Gm. gave 0.4154 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 34.27 per cent calcium ($\mathrm{Ca}^{++}$).

*Triophos. Lehn and Fink Company.*—A sample weighing 0.5196 Gm. gave 0.0690 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 9.49 per cent calcium ($\mathrm{Ca}^{++}$). A sample weighing 0.6603 Gm. gave 0.0891 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 9.64 per cent calcium ($\mathrm{Ca}^{++}$).

*Precipitated Calcium Phosphate N. F. Schieffiin Co.*—A sample weighing 0.5672 Gm. gave 0.2704 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 34.06 per cent calcium ($\mathrm{Ca}^{++}$). A sample weighing 0.8781 Gm. gave 0.4168 Gm. of calcium oxide ($\mathrm{CaO}$). This corresponds to 33.91 per cent calcium ($\mathrm{Ca}^{++}$).

*Magnesium.*—An accurately weighed sample weighing about 0.5 Gm. was dissolved in 15 cc. of diluted hydrochloric acid. Fourteen cc. of ferric chloride solution were added, then sufficient ammonia water to cause the formation of a permanent precipitate and then enough dilute hydrochloric acid to just dissolve the precipitate. This solution was then warmed and added to a hot. solution of 5 Gm. of sodium acetate in 600 cc. of water. The solution was filtered immediately and washed with hot dilute sodium acetate solution (1 Gm. sodium acetate in 400 cc.) until the filtrate gave no test for magnesium. Fifteen cc. of ammonium chloride solution was added to the filtrate. It was then made alkaline with ammonia water and an excess of sodium phosphate solution was added. The solution was then made strongly alkaline with ammonia water. After standing 24 hours the solution was filtered, the precipitate washed into a clean beaker, and dissolved in diluted hydrochloric acid. A 15 cc. portion of ammonium chloride solution was added. The magnesium was then reprecipitated by making alkaline with ammonia water, adding a few cc. of sodium phosphate and then making strongly alkaline with stronger ammonia water. After standing 24 hours the solution was filtered in a prepared Gooch crucible and the precipitate washed with ammonia water. The crucible was placed in an oven at

100 C. for an hour and then it was heated for several hours to constant weight at 400 C. to 500 C. The precipitate was weighed as magnesium pyrophosphate ($Mg_2P_2O_7$).

*Magnesium Phosphate Tribasic. P. W. R. Co.*—A sample weighing 0.6143 Gm. gave 0.5710 Gm. of magnesium pyrophosphate. This corresponds to 20.29 per cent of magnesium ($Mg^{++}$). A sample weighing 0.5284 Gm. gave 0.4911 Gm. of magnesium pyrophosphate. This corresponds to 20.29 per cent magnesium ($Mg.^{++}$).

*Triophos. Lehn and Fink, Inc.*—A sample weighing 0.5428 Gm. gave 0.3409 Gm. of magnesium pyrophosphate. This corresponds to 13.71 per cent magnesium ($Mg^{++}$). A sample weighing 0.5690 Gm. gave 0.3561 Gm. of magnesium pyrophosphate. This corresponds to 13.66 per cent magnesium ($Mg^{++}$).

*Phosphate.*—About 0.5 Gm. of the tribasic phosphate was dissolved in 15 cc. of diluted nitric acid. The solution was filtered and washed and to it 5 Gm. of ammonium nitrate was added. A portion of ammonium molybdate measuring from 120 cc. to 150 cc. was added. After the solution had stood all night the precipitate was filtered off, washed with diluted nitric acid (1 part diluted nitric acid with 2 parts of water) containing a small amount of ammonium molybdate solution. The precipitate was transferred to a clean beaker and dissolved in ammonia water. A 15 cc. portion of ammonium chloride solution and then an excess of magnesia mixture were added. After the solution had been allowed to stand 24 hours it was filtered and the filter washed with ammonia water. The precipitate was heated in a muffle furnace from room temperature up to 600 C. This took three hours. The precipitate was cooled in a desiccator and weighed as magnesium pyrophosphate ($Mg_2P_2O_7$).

*Calcium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 0.4130 Gm. gave 0.2507 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 51.83 per cent phosphate ($PO_4^{\equiv}$). A sample weighing 0.5197 Gm. gave 0.3170 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 52.08 per cent phosphate ($PO_4^{\equiv}$). A sample weighing 0.6294 Gm. gave 0.3827 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 51.91 per cent phosphate ($PO_4^{\equiv}$). A sample weighing 0.4948 Gm. gave 0.3002 Gm. of magnesim pyrophosphate. This corresponds to 51.80 per cent phosphate ($PO_4^{\equiv}$).

*Magnesim Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 0.3382 Gm. gave 0.2133 Gm. of magnesium pyrophosphate. This corresponds to 53.85 per cent of phosphate ($PO_4^{\equiv}$). A sample weighing 0.2432 Gm. gave 0.1535 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 53.89 per cent of phosphate ($PO_4^{\equiv}$).

*Triophos. Lehn and Fink, Inc.*—A sample weighing 0.3618 Gm. gave 0.2154 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 50.67 per cent of phosphate ($PO_4^{\equiv}$). A sample weighing 0.3420 Gm. gave 0.2030 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 50.83 per cent of phosphate ($PO_4^{\equiv}$).

*Precipitated Calcium Phosphate, N. F. Schiefflin.*—A sample weighing 0.4740 Gm. gave 0.2956 Gm. of magnesium pyrophosphate

($Mg_2P_2O_7$). This corresponds to 53.24 per cent phosphate ($PO_4^{\equiv}$). A sample weighing 0.3379 Gm. gave 0.2098 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$). This corresponds to 53.01 per cent of phosphate ($PO_4^{\equiv}$).

*Sulphate.*—About 1 Gm. of tribasic phosphate accurately weighed was dissolved in 15 cc. of diluted hydrochloric acid. The solution was filtered and the filter washed with water. An excess of barium chloride solution was added and the solution was allowed to stand on the water bath for an hour. The precipitate was then filtered in a prepared Gooch crucible, dried at 100 C. and weighed.

*Calcium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 0.9214 Gm. gave 0.0221 Gm. of barium sulphate. This corresponds to 0.97 per cent sulphate ($SO_4^{=}$). A sample weighing 1.0541 Gm. gave 0.0244 Gm. of barium sulphate. This corresponds to 0.95 per cent sulphate ($SO_4^{=}$).

*Triophos. Lehn and Fink, Inc.*—A sample weighing 0.9648 Gm. gave 0.0204 Gm. of barium sulphate. This corresponds to 0.87 per cent sulphate ($SO_4^{=}$). A sample weighing 1.0526 Gm. gave 0.0213 Gm. of barium sulphate. This corresponds to 0.83 per cent of sulphate ($SO_4^{=}$).

*Precipitated Calcium Phosphate, N. F. Schiefflin & Co.*—A sample weighing 1.2940 Gm. gave 0.0346 Gm. of barium sulphate. This corresponds to 1.09 per cent sulphate ($SO_4^{=}$). A sample weighing 1.2822 Gm. gave 0.0343 Gm. of barium sulphate. This corresponds to 1.09 per cent sulphate ($SO_4^{=}$).

*Carbonate.*—The apparatus used was the Knorr apparatus connected with an absorption train consisting of a sulphuric acid filled Geissler bulb, a Geissler bulb containing 50 per cent potassium hydroxide solution, another Geissler bulb containing 50 per cent potassium hydroxide solution and fitted with a water absorbing unit in the form of a tube filled with fused calcium chloride. This tube was connected to a guard tube filled with calcium chloride and this in turn was connected to an aspirator.

About 5 Gm. of tribasic phosphate accurately weighed was introduced into the flask of the Knorr apparatus. The carbon dioxide absorbing bulbs and the first (inside) calcium chloride tube were weighed, connected to the Knorr apparatus with the soda lime guard tube attached and then about three liters of air were drawn through. The aspirator was stopped for a short time. The stop cock on the Knorr apparatus was closed, the soda lime tube disconnected, the reservoir filled with diluted hydrochloric acid and sufficient allowed to enter the flask so that the remainder of 70 cc. of diluted hydrochloric acid would just refill the reservoir and the soda lime tube was replaced. Then the acid was allowed to enter slowly, the aspirator being started and adjusted to make the addition of acid run smoothly. When the acid had all entered the flask the stop cock was closed and heat applied gently to the flask until no bubbles of gas were drawn through the absorption train by the aspirator while the contents of the flask were boiling. The heating was then stopped and the stop cock opened while about 3 liters of air were drawn through. The absorption train was then disconnected, the ends plugged, allowed to come to constant weight in the balance case and then weighed.

*Calcium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 6.2877 Gm. gave 0.0175 Gm. of carbon dioxide ($CO_2$), which corresponds to 0.38 per cent carbonate ($CO_3^{=}$). A sample weighing 5.7252 Gm. gave 0.0175 Gm. of carbon dioxide ($CO_2$), which corresponds to 0.41 per cent carbonate.

*Magnesium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 5.6797 Gm. gave 0.0144 Gm. of carbon dioxide ($CO_2$), which corresponds to 0.34 per cent carbonate ($CO_3^{=}$). A sample weighing 4.5854 Gm. gave 0.0116 Gm. of carbon dioxide, which corresponds to 0.34 per cent carbonate ($CO_3^{=}$).

*Triophos. Lehn and Fink, Inc.*—A sample weighing 5.6368 Gm. gave 0.0594 Gm. of carbon dioxide ($CO_2$), which corresponds to 1.43 per cent carbonate ($CO_3^{=}$). A sample weighing 4.9487 Gm. gave 0.0515 Gm. of carbon dioxide ($CO_2$), which corresponds to 1.41 per cent carbonate ($CO_3^{=}$).

*Precipitated Calcium Phosphate, N. F. Schiefflin Company.*—A sample weighing 5.9277 Gm. gave 0.0225 Gm. of carbon dioxide ($CO_2$), which corresponds to 0.51 per cent carbonate ($CO_3^{=}$). A sample weighing 6.7214 Gm. gave 0.0291 Gm. of carbon dioxide ($CO_2$), which corresponds to 0.59 per cent carbonate ($CO_3^{=}$).

*Calcium Oxide and Magnesium Oxide.*—An accurately weighed sample of about 3 Gm. was weighed in a flat type weighing bottle. The bottle was allowed to stand for sixteen hours with the cover removed in a moving atmosphere of almost pure carbon dioxide. It was then placed in a gently moving stream of air for six hours. The cover was replaced and the bottle reweighed.

*Calcium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 3.3623 Gm. gained 0.0251 Gm. This is the equivalent of 0.95 per cent calcium oxide.

*Magnesium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 2.3904 Gm. gained 0.0072 Gm. This is the equivalent of 0.27 per cent magnesium oxide.

*Triophos. Lehn & Fink, Inc.*—A sample weighing 3.3344 Gm. gained 0.0249 Gm. This is the equivalent of 0.95 per cent calcium oxide.

*Precipitated Calcium Phosphate, N. F. Schiefflin Company.*—A sample weighing 4.3933 Gm. gained 0.0171 Gm. This is the equivalent of 0.49 per cent calcium oxide.

This method of procedure was designed to determine the amount of uncombined calcium oxide or magnesium oxide present in calcium or magnesium tribasic phosphate in the "dry way" as it was feared that any water added might give opportunity for reactions that would entirely obscure the presence of either of these compounds. Further investigation of this method at the suggestion of Dr. Rosin of the Powers-Weightman-Rosengarten Co. indicated that this method would not give sufficiently comparable results. It might give rough quantitative results if a large amount of one of the oxides was present.

*Hydrochloric Acid Insoluble Portion.*—The portion insoluble in hydrochloric acid was determined by adding hydrochloric acid to a weighed portion and filtering, drying at 100 C. and weighing the insoluble residue. The Powers-Weightman-Rosengarten products contained only a trace of insoluble material.

*Triophos. Lehn & Fink, Inc.*—A sample weighing 0.5912 Gm. left an insoluble residue weighing 0.0020 Gm. This represents 0.33 per cent hydrochloric acid insoluble material.

*Precipitated Calcium Phosphate. Schiefflin Company.*—A sample weighing 0.6670 Gm. left an insoluble residue weighing 0.0015 Gm. This represents 0.22 per cent hydrochloric acid insoluble material.

*Loss in Weight at 200 C.*—About 1 Gm. accurately weighed was heated in an oven at 200 C. The samples never came to constant weight and even gained in weight at times. The value recorded was a value showing a fairly high amount of moisture and occurred a large number of times in more than thirty weighings.

*Calcium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 0.8068 Gm. lost 0.0359 Gm. This is equivalent to 4.45 per cent.

*Magnesium Phosphate Tribasic. Powers-Weightman-Rosengarten Co.*—A sample weighing 1.4693 Gm. lost 0.2721 Gm. This is equivalent to 18.51 per cent.

*Triophos. Lehn & Fink, Inc.*—A sample weighing 0.7476 Gm. lost 0.1186 Gm. This is equivalent to 15.86 per cent.

*Precipitated Calcium Phosphate N. F. Schiefflin Company.*—A sample weighing 0.9985 Gm. lost 0.0510 Gm. This is equivalent to 5.10 per cent.

## CARBOHYDRATE IN CERTAIN "DIABETIC" FLOURS

The Council on Pharmacy and Chemistry requested the Laboratory to determine whether or not Lister's Prepared Casein Diabetic Flour and Diaprotein Diabetic Flour were free from sugar and starch as claimed on the label. A specimen of each of these two products was purchased on the open market.

A sample of each was treated with water acidulated with hydrochloric acid for one hour at a temperature of 90 to

100 C.; filtered, made alkaline with sodium hydroxide and tested for carbohydrates with the modified Haines' solution. No reduction took place.

At the same time soycasein flour (which had been submitted to the Council) had been treated in the same manner. Reducing substances were found.

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## DEXTROSE (CERELOSE) LILLY

A specimen of Dextrose (Cerelose) and 2 ampoules of "Glucose 50% Solution Lilly" (Eli Lilly and Co.) were submitted to the Laboratory for examination. At a later date six more ampoules of the solution were received.

### Dextrose (Solid)

This product was a finely granular, white, odorless powder of good appearance. Its solution in water (1-20) was colorless but contained small amounts of suspended matter. The specimen was found to comply with all of the tests for identity and purity proposed for New and Nonofficial Remedies 1925. It contained a minute trace of chloride, and a noticeable amount of sulphate. The limit of sulphate permitted by the test proposed for Dextrose in the U. S. Pharmacopeia X, was exceeded; traces of calcium were present.

The quantitative results obtained were as follows:

| | | |
|---|---|---|
| Loss at 100 C. | 1.63 | per cent |
| Ash | 0.045 | per cent |
| [*]Sulphate (as $H_2SO_4$) | 0.05 | per cent |
| $\alpha$ at 25 C. | 52.69 | per cent |

[*] Limit proposel for U. S. Pharmacopeia X is equivalent to 0.025 per cent of $H_2SO_4$.

The substance conforms to the tests proposed for New and Nonofficial Remedies, although it contains more sulphate than is permitted by the U. S. Pharmacopeia X. The product was found to be of a satisfactory degree of purity to be admitted to New and Nonofficial Remedies.

### Ampoules Glucose Lilly

The preparation was a pale greenish-yellow, clear solution having a cresol-like odor. It was stated to contain 0.1 per cent of cresol as a perservative and an unstated amount of "buffer salts." Each ampoule was stated to contain 20 cc. of a solution and the solution was claimed to be a 50 per cent solution.

The quantitative results obtained were as follows:

| | | |
|---|---|---|
| Specific gravity at 25 C | 1.1978 | |
| Solids at 100 C | 44.87 | per cent |
| Dextrose (by rotation) | 40.39 | per cent |
| Dextrose (by copper reduction Difren-O'Sullivan Method) | 46.94 | per cent |
| Sulphuric acid ($H_2SO_4$) | 0.023 | per cent |
| Ash | 0.34 | per cent |

The preparation contained sulphate greater than the U. S. Pharmacopeia X permits for dextrose (based upon the solid content). The ash content (0.34 per cent) was excessive; the excess ash, however, is most likely due to the "buffer salts" stated to be present; tests indicated the presence of phosphate ($PO_4^{---}$).

It will be noted that there is a variance in the results obtained for solids, dextrose by copper reduction and dextrose by rotation. The Laboratory inquired if Lilly & Co. could offer any explanation of this discrepancy.

[Note.—Since this was written, Eli Lilly and Co. have submitted new specimens which comply with the U. S. P. standards and also firm's statements of strength and purity. These latter are what are being marketed. The discrepancy in the two methods of determination has been pointed out in the literature since this has gone to press. (See Jour. Biol. Chem., July, 1926, p. 1.)]

## IODINIZED LIQUID PETROLATUM

Four 500 cc. bottles of "Iodinized Liquid Petrolatum (Wm. Joseph Schepherd, New York)" were submitted to the Laboratory for analysis. According to the labels, these four bottles were claimed to contain U. S. P. resublimed iodine in given but varying amounts dissolved in specially refined mineral oil.

The free iodine content was determined in the following way: 50 cc. of the solution was titrated with tenth normal sodium thiosulphate solution in the presence of 25 cc. of 10 per cent potasium iodide solution. Starch was used as an indicator at the end of the titration. The fading of the well known starch iodide color was the end point. Vigorous shaking was employed to hasten the transfer of the iodine from the oil into the potassium iodide solution.

Analysis

| Number Cc. Taken | Specific Gravity | Number Cc. N/10 Sodium Thiosulphate Solution Required | Per Cent Found | Per Cent Claimed |
|---|---|---|---|---|
| 50 | 0.8760 | 16.58 | 0.48 | 1.25 |
| 50 | 0.8760 | 16.60 | 0.48 | 1.25 |
| 50 | 0.8725 | 17.88 | 0.52 | 1.00 |
| 50 | 0.8725 | 18.08 | 0.52 | 1.00 |
| 50 | 0.8623 | 22.54 | 0.66 | 0.75 |
| 50 | 0.8623 | 22.60 | 0.66 | 0.75 |
| 50 | 0.8720 | 18.98 | 0.55 | 0.50 |
| 50 | 0.8720 | 19.03 | 0.55 | 0.50 |

The deficiency in the amount of available iodine in three of the specimens submitted was reported to the Council on Pharmacy and Chemistry.

## LARVEX

Larvex is the name of the proprietary article sold as a moth preventative by the Larvex Corporation, New York.

According to the directions, woolen fabrics may be sprayed with this solution, thereby rendering them immune to attacks from moths. Previous to April, 1923, the declaration on the label showed that the product contained arsenic as the active ingredient. In the April 14, 1923, issue of The Journal an editorial pointed out the danger of the continued use of such a potent substance as arsenic as a preventative for moth damage, particularly when no warning is given to the final purchaser of the fabrics concerning its presence. Subsequently The Journal was informed by the firm that the formula had been changed and that the preparation now contains "fluorides with certain bitter principals from plants, not alkaloids." Quantitative data were not given nor was the full identity of the ingredients declared. The firm also submitted a request for advertising space in The Journal. The Advertising Committee therefore asked the Laboratory to determine if the product contained substances which might be injurious to health.[1]

Accordingly one original specimen of Larvex Solution received from the Larvex Corporation, September, 1923, was examined for its fluoride content. Quantitative determinations showed that the amount of fluoride present was equivalent to 0.28 per cent of sodium fluoride. Alkaloids were absent. Only a trace of arsenic was found.

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[1] Other evidence was also asked of the firm, which was not supplied; the product, therefore, never came up for final consideration by the Advertising Committee and hence was never advertised in The Journal.

## Details of Analysis

*Fluoride.*—Fluoride was determined as calcium fluoride according to the method as given in Analytical Chemistry by Treadwell and Hall, Volume II, 4th edition, p. 471. The method is as follows:

> If the solution contains free hydrofluoric acid or an acid fluoride, sodium carbonate is added until the reaction is alkaline and from one fourth to one fifth as much more in excess.* To solutions of neutral fluorides about 1 cc. of double-normal sodium carbonate solution is added. The alkaline solution is heated to boiling, precipitated by means of an excess of calcium chloride solution, filtered, and thoroughly washed with hot water. The precipitate consisting of the fluoride and carbonate of calcium is dried, as much of it as possible is transferred to a platinum crucible, the ash of the filter is added, and the contents of the crucible are ignited.† After cooling, the mass is covered with an excess of dilute acetic acid, by which the lime is changed to the soluble acetate, while the fluoride is unaffected. After evaporating to dryness on the water-bath, the mass is taken up in water, filtered, washed and dried.‡ After transferring as much of the dried precipitate to the crucible as possible, the filter-paper is burned, its ash added, and after ignition the crucible is again weighed. To confirm the result the substance is treated with a little concentrated sulphuric acid (added cautiously), and after evaporating off the excess of the latter and once more igniting, the contents of the crucible are weighed as calcium sulphate.

1 Gm. $CaF_2$ yields 1.7436 Gm. $CaSO_4$.

(a) Twenty-five cc. of Larvex yielded 0.0992 Gm. of calcium fluoride, equivalent to 0.28 per cent of sodium fluoride.

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* By the addition of the excess of sodium carbonate the precipitate of calcium fluoride will contain calcium carbonate, and presence of the latter renders the precipitate easy to filter. A pure precipitate of calcium fluoride is so slimy that the pores of the filter become so clogged that it is almost impossible to complete the filtration.

† The ignition makes the $CaF_2$ denser and hence easier to filter.

‡ The calcium fluoride is not volatilized in an open platinum crucible heated over a Bunsen burner. Heated over the blast, there is appreciable volatilization.

(b) Twenty-five cc. yielded 0.1006 Gm. calcium fluoride, equivalent to 0.28 per cent sodium fluoride. The calcium fluoride was converted to calcium sulphate, which confirmed the results.

## MERCURIC OXYCYANIDE SOLUTION, SWAN-MYERS

Mercuric Oxycyanide Solution, Swan-Myers, was submitted to the Laboratory for examination by the Council on Pharmacy and Chemistry. It is marketed in three different strengths of ¼ gr., ⅙ gr. and ⅛ gr. in 5 cc., respectively. Analysis of the product was as follows:

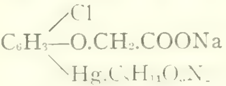
| | Amount Declared | Amount HgOHg $(CN)_2$ Found | Percent HgO Ratio Found | N.N.R. Requirements | Percent $Hg(CN)_2$ Ratio Found | N.N.R. Requirements |
|---|---|---|---|---|---|---|
| Mercuric oxycyanide ¼ gr. | 0.25 gr. | (a) .27 | 40.1 | 44.3 to | 59.9 | 51.7 to |
| | | (b) .27 | 41.1 | 48 | 58.9 | 56.0 |
| Mercuric oxycyanide ⅙ gr. | 1.66 gr. | (c) .18 | 40.3 | | 59.7 | |
| | | (d) .18 | 40.3 | | 59.7 | |
| Mercuric oxycyanide ⅛ gr. | 0.125 | (e) .14 | 39.6 | | 60.4 | |
| | | (f) .14 | 39.6 | | 60.4 | |

The method employed was that described in New and Nonofficial Remedies, 1925, except that 10 cc. of the solutions was used for the assay. The amount of mercuric oxycyanide present as $HgO.Hg(CN)_2$ is fairly close to the declared amount. The amount of HgO in ratio to $Hg(CN)_2$ is considerably lower than the figures given in New and Nonofficial Remedies. It is probable that when the firm's attention is called to this, the mercuric oxide content will be increased; as it is, it is doubtful if the lower amount found is of therapeutic importance.

## NOVASUROL

Novasurol was submitted to the Council on Pharmacy and Chemistry by the Winthrop Chemical Company, New York. It is sold only in solution in ampules, but on request some of the solid substance was obtained from the manufacturers for examination.

According to the label, Novasurol[1] is "The double salt of sodium-oxymercurio-chlorophen-oxylacetate with diethyl-barbituric acid." The formula as supplied by the manufacturer is:



$$C_6H_3\begin{cases}Cl\\ O.CH_2.COONa\\ Hg.C_8H_{11}O_3N_2\end{cases}$$

The A. M. A. Chemical Laboratory was asked for an opinion. It reported to the Council as follows:

1. The diethylbarbituric acid is probably bound to the mercury compound, but not firmly. On acidulating a concentrated solution of Novasurol with diluted hydrochloric acid, and shaking immediately with ether, diethylbarbituric acid may be obtained. The diethylbarbituric acid cannot be obtained quantitatively by this method because of interference of chloro-phenyloxyacetic acid. The product responded to most of the qualitative tests supplied by the manufacturer.

2. The mercury does not respond to ordinary reactions for mercury in the cold. For instance mercury sulphide is not precipitated by hydrogen sulphide from a solution of Novasurol in the cold.

3. The amount of moisture in the specimen submitted was 1.97 per cent.

4. According to theory, the compound should contain 33.86 per cent of mercury. Found (a) 33.42 per cent of mercury (Hg); (b) 33.55 per cent in the undried specimen, equivalent to (a) 34.09 per cent and (b) 34.22 per cent in the dried sample. Average, 34.15 per cent. The method of assay furnished by the manufacturer did not give comparable results. Modifications of the method, after precipitation by hydrogen sulphide, in general accordance with the U. S. Pharmacopeia IX directions, is essential.

5. A weighed sample was treated with sulphuric acid in a platinum dish and the residue, after further treatment with sulphuric acid and heat, was weighed as sodium sulphate. The amount of sodium found according to this method was (a) 3.87 per cent; (b) 3.91 per cent. Average, 3.89 per cent. Theory, 3.90 per cent.

6. From both the mercury and the sodium determinations the compound may be considered to have the empiric formula as claimed, the mercury and sodium being in molecular proportions.

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[1] According to Frankel and other sources, *Asural* is a double salt of sodium oxy-mercuri-salicylate and sodium amino-oxybutyrate. The new product Novasurol represents, therefore, quite a marked modification in constitution.

7. The manufacturers state that the product does not give a precipitate with albumin. Using a solution of fresh egg albumin (1 : 5) a precipitate was formed on addition to Novasurol solution.

## Novasurol Ampules

The liquid in the ampules (made of colored glass) had a strong odor resembling guaiacol, the presence of which is not declared. Also the mercury does not seem to be in as firmly bound condition as a fresh solution made from the solid Novasurol. On treating with ammonium sulphide *in the cold* the liquid yielded a precipitate in 2 or 3 minutes. In case of fresh solution, this did not occur for some time. The solution in the ampules also yielded a precipitate with a solution of fresh egg albumin.

As a result of this work, and after correspondence with the distributor, at the request of the Council, the Laboratory prepared the following standards to be published in New and Nonofficial Remedies:

**NOVASUROL.**—Merbaphen. The double salt of sodium mercurichlorphenyl oxyacetate with diethylbarbituric acid — $(NaOOCCH_2.O).Cl.C_6H_3.Hg[\underline{CO:NCO.C(C_2H_5)_2CONH}]$. Novasurol contains 33.9 per cent of mercury.

Novasurol occurs as a white crystalline powder, odorless; soluble in cold water. The solution is slightly alkaline. Addition of strong acids to a solution of novasurol yields a precipitate consisting of diethyl barbituric acid, and the mercury derivative of chloro-phenyloxyacetic acid; on heating the solution the latter breaks up to mercuric chloride and chloro-phenyloxyacetic acid.

To 2 cc. of a solution of novasurol (1 in 1,000) add 0.1 cc. of ferric chloride solution (1 in 25): a flesh colored precipitate forms. Add ammonium sulphide solution to 10 cc. of novasurol 5 per cent: there is developed slowly when cold, and quickly when heated, a black discoloration of the liquid with later formation of a black precipitate of mercuric sulphide. Add 2 cc. of sodium hydroxide solution to 5 cc. of novasurol solution 5 per cent: no precipitate forms. Add 1 cc. of solution of formaldehyde and heat: metallic mercury separates from the solution.

Dry about 1 Gm. of novasurol, accurately weighed, for six hours at 100 C.: the loss in weight is not more than 2 per cent.

Transfer about 0.7 Gm. of novasurol, accurately weighed, to an Erlenmeyer flask; add 100 cc. of water and agitate until powder has dissolved; add 15 cc. of strong hydrochloric acid, connect to a reflux condensor and boil for three hours. Add 175 cc. of hot water, and pass in hydrogen sulphide for fifteen minutes. (It is important that the temperature of the solution should be about 70 C. in order to keep in solution slightly soluble organic compounds formed during hydrolysis.) Filter while warm, through a Gooch crucible, wash with distilled water and finally three portions of cold alcohol and then one portion of carbon disulphide. Close the rubber tubing leading from the suction flask to the suction pump with a pinch clamp; add sufficient carbon disulphide to cover the precipitate, cover the crucible with a watch glass and allow to stand one-half hour. Then release pinch clamp, drain off solution and wash with several portions of carbon disulphide. Dry in an oven at 100 C. for four hours. Weigh the mercuric sulphide and calculate to mercury: the mercury content of the dried specimen is not less than 33 per cent nor more than 34.5 per cent.

Place about 0.5 Gm. of novasurol, accurately weighed, in a tared platinum dish, add 10 cc. of sulphuric acid and gently heat while fumes of sulphur trioxid are evolved. (The mercury is also volatilized.) Cool in desiccator and weigh as sodium sulphate: the sodium calculated from this determination should not be more than 4.0 per cent, nor less than 3.75 per cent.

## Details of Analysis

*Moisture.*—An accurately weighed sample was dried in an electric oven for fifteen hours at 100 C.; the loss in weight of 0.9627 Gm. of sample was 0.0190 Gm., equivalent to 1.97 per cent.

*Mercury.*—Efforts were made to determine the mercury electrolytically after acid and alkali treatment. The results were not satisfactory and this method was not pursued further.

The method furnished by the manufacturer was:

> "25 cc. of the 10 per cent solution is diluted with 75 cc. water, and after addition of 30 cc. hydrochloric acid (specific gravity 1.124) is kept at a boiling temperature for four hours in an Erlenmeyer flask with reflux condenser. Water is then added up to about 300 cc. and the mercury precipitated by introduction of hydrogen sulphide at about 70 C. This is removed by suction, carefully washed, dried at 100 C. and weighed. The number of grams of mercury sulphide obtained, multiplied by 3.448, gives the quantity of mercury in 100 cc. This should amount to about 3.39 Gm."

(a) 0.7612 Gm. was dissolved in 90 cc. of water and 15 cc. of hydrochloric acid added. The flask was then attached to a reflux condenser and contents boiled for three hours. After removal from the condenser 150 cc. of cold water was added and hydrogen sulphide passed in the solution for 15 minutes. The flask was then stoppered, allowed to stand overnight, then saturated with hydrogen sulphide again next morning and filtered. The residue was treated with carbon disulphide. The weight of mercuric sulphide was 0.3261 Gm., equivalent to 36.92 per cent. This result was too high. It was thought that the high result was due to the presence of some hydrolized by-products which separated out from the cooled solution overnight. Therefore, in the next two determinations the sulphide was precipitated while hot and the solution filtered while hot.

(b) 0.5196 Gm. of sample was treated exactly as described in the assay for the proposed monograph. The weight of the mercuric sulphide was 0.2015 Gm., equivalent to 33.42 per cent mercury in the sample or 34.09 per cent in the dried substance.

(c) 0.9627 Gm. of the sample treated as in "B" yielded 0.3679 Gm. of mercuric sulphide, equivalent to 33.55 per cent mercury in the sample or 34.22 per cent in the dried specimen.

*Sodium.*—A weighed sample was treated with sulphuric acid in a platinum dish, heated over an electric heater until practically dry, and treated subsequently as described in the proposed monograph. (a) 0.5185 Gm. yielded 0.0619 Gm. of sodium sulphate, equivalent to 3.87 per cent sodium in the sample or 3.94 per cent calculated for the dried specimen; (b) 0.5603 Gm. yielded 0.0674 Gm. of sodium sulphate, equivalent to 3.91 per cent sodium in the sample or 3.98 per cent calculated for the dried specimen. Theory, 3.90 per cent sodium.

## PERL-O-DENT

In the submission of Perl-O-Dent Mouth and Throat Wash, Perl-O-Dent Chemical Company, Milwaukee, to the Council on Pharmacy and Chemistry, the preparation was stated to be made as follows:

> "Glycerine 16 ounces to which is added 1 ounce of oil of wintergreen which is thoroughly mixed; to this is added 3 ounces of iodine and allowed to stand from twelve to fourteen hours until the glycerine has absorbed its quota of the iodine. To this solution is added 90 ounces of water (by graduate measure) a heavy precipitate is thrown down. This final preparation is again allowed to stand from twelve to fourteen hours and is then put through the process of filtration until all of the precipitate and cloudiness disappears.

The preparation was claimed to depend on iodine for its effects but the amount of free iodine was not declared.

Tests showed the presence of both free iodine and iodide. The amount of free iodine was found to be 0.11 per cent; although the firm declared that "our preparation is not an iodide," the amount of iodide present (calculated from iodine liberated by ferric ions) was found to be 0.34 per cent ($I^-$).

## SOLARSON

Solarson (Solution of chlorarsenol, 1 per cent) marketed by the Winthrop Chemical Co., is stated to be a 1 per cent ammonium heptenchlorarsonate ($CH_3(CH_2)_4.CCl:CH.As.O.(OH)(ONH_4)$). Along with other tests made at the time of its submission to the Council, it was analyzed for arsenic.

A sample measuring 1 cc. was pipetted from a freshly opened ampule into a 50 cc. volumetric flask. The sample was diluted to exactly 50 cc. A 25 cc. aliquot was poured into the thistle tube of the hydrogen generator of a Marsh apparatus that had shown on a fifteen minute run that it was generating arsenic free hydrogen. The arsenic was collected in a fused silica arsenic tube. The determination was considered to be complete when no stain was found on a clean portion of the tube after a fifteen minute test, the burner being appropriately placed and adjusted. Each run lasted from one hour to two hours and a half.

Three different ampules were analyzed. The weights of the collected arsenic were 0.0010 Gm., 0.0009 Gm. and 0.0009 Gm., respectively. The distributors claim about 0.0030 Gm. per cc. (or about 0.0015 Gm. per ½ cc.).

The results were submitted to the distributor, who asked Dr. Gettler of the New York University Medical School to determine the arsenic.

He modified the method and obtained an average of 2.75 mg. of arsenic in 1 cc. of solution.

The A. M. A. Chemical Laboratory then made more arsenic determinations using a method that differed from that of Dr. Gettler only in the method of obtaining the sample. The method used is as follows:

About 1 cc. of a freshly opened ampule was pipetted into a small glass stoppered weighing bottle. The sample was weighed and then washed into a Kjeldahl flask. To it were added 5 cc. of arsenic free nitric acid and 5 cc. arsenic free sulphuric acid. The solution was boiled until fumes of sulphur trioxide appeared. When the solution became cool water was added and the solution boiled for five minutes. The solution was cooled and made up to exactly 100 cc. in a volumetric flask.

Fifty cc. of this solution were added in portions to a previously started Marsh apparatus. The arsenic was collected in a fused silica arsenic tube 15 cm. long. The tube was heated to redness in two places and cooled in two other appropriate places with strips of cloth upon which distilled water was squirted at frequent intervals. Two determinations showed the presence of 2.48 mg. arsenic and 2.63 mg. arsenic, respectively, obtained from 1 Gm. portions of solution. In these determinations the Marsh apparatus was kept running for six hours and six and one-fourth hours, respectively.

As a result of these observations, the Laboratory submitted the following report to the Council:

"The A. M. A. Chemical Laboratory reports that it has reexamined the ampules of Solarson from the same box as those used in the analysis previously reported to you February 26, 1925; this time the method employed was that proposed by Dr. Gettler, except in the slight modification of weighing the sample rather than measuring it. The Laboratory reports that two determinations yielded 2.48 mg. and 2.63 mg. of arsenic, respectively, in one gram portions of the solution. Dr. Gettler reports that in the analysis of the ampules submitted to him, the arsenic content was 2.75 mg. Theory 2.96. The content of Solarson, as based on these analyses is somewhat low, but in the opinion of the laboratory not of a serious nature."

## SPRAY-O-ZONE

An original bottle of Spray-O-Zone (Coral Chemical Co., Inc., Buffalo), was submitted to the Laboratory for preliminary examination. The bottle contained approximately 8 fluid ounces of a colorless, odorless liquid having a bitter salty taste, and an alkaline reaction to litmus. Qualitative tests indicated the presence of potassium, sodium, borate and chlorate ($ClO_3$). Tests for nitrate and ammonia, even in small amounts were negative. The amounts of solids obtained by the evaporation of a 10 cc portion was approximately 7 per cent. The product bears a resemblance to Zyme-Oid and Oxychlorine in that these products contain the same substituents found in Spray-O-Zone; they differ, however, from Spray-O-Zone in that they contain nitrate while nitrate was not found in the latter. Furthermore, Zyme-Oid, and Oxychlorine[*] were solids (the aqueous solutions of which gave acid reactions to litmus) whereas Spray-O-Zone is an alkaline liquid. Extensive qualitative tests and quantitative estimations were not made. From the tests made, it appears that Spray-O-Zone contains essentially borax and potassium chlorate (sometimes sold under the vernacular name, Potash Tablets).

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[*] Also Loeffler's Intravenous Compound.

## THEOCALCIN

Theocalcin, manufactured by E. Bilhuber, Inc., New York, was submitted to the Council on Pharmacy and Chemistry for inclusion in New and Nonofficial Remedies. The Council in turn asked the A. M. A. Chemical Laboratory to investigate the chemical claims. The specimen was a white powder, which gave tests for calcium, sodium, salicylate and theobromine.

According to the circular submitted at that time:

"Theocalcin is the calcium salt of theobromine and salicylic acid of the chemical formula $C_{14}H_{12}N_4O_5Ca$, containing 11 per cent calcium, 48 per cent theobromine, and 38 per cent salicylic acid. It is a white powder, difficultly soluble in water. In Europe Theocalcin is known under the descriptive name of Calcium-Diuretin.

"Theocalcin possesses certain advantages over the sodium compounds of theobromine and other xanthine derivatives in that it is more pleasant to take and, being less soluble, passes the stomach practically unchanged. It, therefore, causes no gastric disturbance or irritation, but is dissolved and absorbed wholly from the intestines. Thus Theocalcin is particularly valuable for long continued medication."

When Theocalcin was treated with 0.2 per cent hydrochloric acid, however, the salicylic acid was split off practically quantitatively. For instance, when 0.6766 Gm. (the dose recommended is 0.5 to 1 Gm.) was treated with 67 cc. of 0.2 per cent hydrochloric acid, extracted in usual manner with ether, the amount of salicylic acid recovered was 35.4 per cent. In another experiment using 1.7053 Gm. Theocalcin and 170 cc. of 0.2 per cent hydrochloric acid, the amount recovered was 37.8 per cent. In this respect, the product behaves like "Theobromine sodium and sodium salicylate."

Another advantage claimed is insolubility in water; this was also determined. It was found that the product when treated with water was soluble to the extent of approximately 80.0 per cent. For instance (a) 0.5534 Gm. was shaken for 15 minutes with 50 cc. of water at room temperature; the amount dissolved was 78.5 per cent; (b) 1.7411 Gm. was treated with 120 cc. of water for 30 minutes; the amount dissolved was 79.8 per cent.

Because of these variances with the claims, it was thought well to determine whether the product being examined was of the composition stated. The following table shows that it was in substantial agreement with the claimed composition.

| | Claimed, Per Cent | Found, Per Cent |
|---|---|---|
| Calcium | 11 | 11.35 |
| Salicylic acid | 38 | 37.3 |
| Theobromine | 48 | 43.5 |
| Moisture | .. | 0.8 |

From the foregoing it is evident that Theocalcin is *not* "difficultly soluble in water" and that it does not pass "the stomach practically unchanged." When these and other objections were brought to the firm's attention by the Council, the firm revised its statements. Subsequently the product was found acceptable for New and Nonofficial Remedies, under the following description:

**THEOCALCIN.**—A double salt or mixture of calcium theobromine ($[C_7H_7O_2N_4]_2Ca$) and calcium salicylate ($[C_7H_5O_3]_2Ca$). It contains not less than 44 per cent of theobromine.

Theocalcin is a white, amorphous powder, having a saline taste. It is partly soluble in water.

An aqueous solution of theocalcin is alkaline to phenolphthalein. An aqueous solution of theocalcin (1 in 100), slightly acidulated with acetic acid, becomes violet on the addition of ferric chloride solution. Transfer about 0.05 Gm. of theocalcin to a test tube, add 3 cc. of diluted acetic acid and heat to boiling; cool the contents of the test tube, filter and to the filtrate add 0.5 cc. of ammonium oxalate solution: a precipitate forms, which dissolves on addition of 1 cc. of diluted hydrochloric acid. To about 0.05 Gm. of the precipitate obtained in the assay for theobromine, add 1 cc. of hydrochloric acid and about 0.1 Gm. of potassium chlorate and evaporate to dryness on a water bath: a reddish yellow residue remains, which becomes purple when moistened with a drop of ammonia water.

Dried to constant weight at 110 C., theocalcin loses not more than 5 per cent (*water*). Treat 0.1 Gm. theocalcin with 2 cc. of sulphuric acid: no effervescence occurs (*carbonate*) nor is more than a slight color produced (*readily carbonizable substances*). Mix 1 Gm. of theocalcin with 10 cc. of distilled water, add a few cubic centimeters of sodium hydroxide solution (filter if necessary) and shake the mixture with 10 cc. of chloroform, separate the chloroform layer, evaporate it to dryness on a water bath and dry to constant weight at 80 C.: the weight of the residue so obtained does not exceed 0.005 Gm. (*caffeine*).

Suspend about 2 Gm. of theocalcin, accurately weighed, in 75 cc. of water and add diluted hydrochloric acid until the solution is acid to phenolphthalein. Warm gently, then add sodium carbonate solution until the calcium is completely precipitated, avoiding a large excess. Filter off the calcium carbonate; evaporate the combined filtrate and washings on a steam bath to 20 cc. Add diluted hydrochloric acid, drop by drop, until just acid (to phenolphthalein), then dilute ammonia water until slightly alkaline. Allow to stand at from 20 to 25 C. for three hours, stirring occasionally. Transfer the precipitate of theobromine to a tared Gooch crucible. Wash the precipitate and filter with four successive portions of 5 cc. each of ice cold distilled water and dry to constant weight at 100 C. To the weight of the precipitate thus obtained, add 0.14 Gm. The total weight corresponds to not less than 44 per cent of the weight of theocalcin taken. About 0.2 Gm. of the precipitate obtained in the assay for theobromine volatilizes when slowly heated, leaving only a negligible residue.

## BOAL'S ROLLS

### Another Phenolphthalein Laxative "Fruit"

Boal's Rolls, sold by Boal's Rolls Corporation of New York, is claimed to be "real fruit medicated." No information was given on the label concerning the nature of the medication.

The preparation consisted of large tablets weighing about 7 Gm. (100 grains) each which had a distinct odor and taste of figs. Qualitative tests indicated the presence of starch, figs and phenolphthalein.

## BALZONE

Balzone, manufactured by N. L. Waelchli of Denver, was submitted to the Laboratory for examination. The ingredients of the "Balzone Method" were in two packages—a 16 ounce bottle and a half-ounce bottle, the latter only partially filled. The contents of the larger bottle consisted of an odorless, pink liquid. Preliminary tests indicated that this contained no potent ingredients but that it had the physical and chemical properties of ordinary water which had been colored pink.

The half-ounce bottle contained a pale yellow liquid which appeared to consist of a volatile oil similar in odor and consistency to some of the pine oils. As the quantity of material was too small for analysis, no further tests were carried out. According to the circular of directions accompanying the "Balzone Method" of treatment the method consists in heating some of the pink water to which a few drops of the volatile oil have been added and inhaling the vapor.

## HARRIET HUBBARD AYER'S FACE CREAM

An original sample of "Face Cream" manufactured by Harriet Hubbard Ayer, New York, was submitted to the Laboratory for examination as to presence of metallic substances.

Qualitative tests showed the presence of ammoniated mercury; zinc oxide was also present. The New Hampshire state chemists analyzed Ayer's Face Cream and in a bulletin, issued in 1918, reported on it as follows: "Submitted with complaint that its use seemed to cause puffiness under eyes, burning of skin, and eruptions. Is a rose-scented white ointment, the constituents of which include zinc oxide and a compound of mercury. User advised of dangerous character and the necessity for caution in applying."

## TYPE CLEANER

A sample of type cleaner, submitted to the Laboratory by the A. M. A. Press, was found to be a suspension of paraffin in a saturated solution of paraffin in benzene. The paraffin present amounted to 4.07 per cent or about 1 part in 24½ by weight. The ash was very small.

## FORMET

A sample of Formet was submitted to the Laboratory by the A. M. A. heating plant for examination. It appeared to be essentially a solution of sodium silicate (water glass). No other constituents in more than negligible amounts were found except that of the chloride ion.

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